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TABLE OF CONTENTS

[Intervention Review]

Medical treatments for incomplete miscarriage

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ABSTRACT

Background

Miscarriage occurs in 10% to 15% of pregnancies. The traditional treatment, after miscarriage, has been to perform surgery to remove any remaining placental tissues in the uterus ('evacuation of uterus'). However, medical treatments, or expectant care (no treatment), may also be effective, safe, and acceptable.

Objectives

To assess the effectiveness, safety, and acceptability of any medical treatment for incomplete miscarriage (before 24 weeks).

Search methods

We searched Cochrane Pregnancy and Childbirth's Trials Register (13 May 2016) and reference lists of retrieved papers.

Selection criteria

We included randomised controlled trials comparing medical treatment with expectant care or surgery, or alternative methods of medical treatment. We excluded quasi-randomised trials.

Data collection and analysis

Two review authors independently assessed the studies for inclusion, assessed risk of bias, and carried out data extraction. Data entry was checked. We assessed the quality of the evidence using the GRADE approach.

Main results

We included 24 studies (5577 women). There were no trials specifically of miscarriage treatment after 13 weeks' gestation.

Three trials involving 335 women compared misoprostol treatment (all vaginally administered) with expectant care. There was no difference in complete miscarriage (average risk ratio (RR) 1.23, 95% confidence interval (CI) 0.72 to 2.10; 2 studies, 150 women, random-effects; very low-quality evidence), or in the need for surgical evacuation (average RR 0.62, 95% CI 0.17 to 2.26; 2 studies, 308 women, random-effects; low-quality evidence). There were few data on 'deaths or serious complications'. For unplanned surgical intervention, we did not identify any difference between misoprostol and expectant care (average RR 0.62, 95% CI 0.17 to 2.26; 2 studies, 308 women, random-effects; low-quality evidence).

Sixteen trials involving 4044 women addressed the comparison of misoprostol (7 studies used oral administration, 6 studies used vaginal, 2 studies sublingual, 1 study combined vaginal + oral) with surgical evacuation. There was a slightly lower incidence of complete miscarriage with misoprostol (average RR 0.96, 95% CI 0.94 to 0.98; 15 studies, 3862 women, random-effects; very low-quality evidence) but with success rate high for both methods. Overall, there were fewer surgical evacuations with misoprostol (average RR 0.05, 95% CI 0.02 to 0.11; 13 studies, 3070 women, random-effects; very low-quality evidence) but more unplanned procedures (average RR 5.03, 95% CI 2.71 to 9.35; 11 studies, 2690 women, random-effects; low-quality evidence). There were few data on 'deaths or serious complications'. Nausea was more common with misoprostol (average RR 2.50, 95% CI 1.53 to 4.09; 11 studies, 3015 women, random-effects; low-quality evidence). We did not identify any difference in women's satisfaction between misoprostol and surgery (average RR 1.00, 95% CI 0.99 to 1.00; 9 studies, 3349 women, random-effects; moderate-quality evidence). More women had vomiting and diarrhoea with misoprostol compared with surgery (vomiting: average RR 1.97, 95% CI 1.36 to 2.85; 10 studies, 2977 women, random-effects; moderate-quality evidence; diarrhoea: average RR 4.82, 95% CI 1.09 to 21.32; 4 studies, 757 women, random-effects; moderate-quality evidence).

Five trials compared different routes of administration, or doses, or both, of misoprostol. There was no clear evidence of one regimen being superior to another.

Limited evidence suggests that women generally seem satisfied with their care. Long-term follow-up from one included study identified no difference in subsequent fertility between the three approaches.

Authors' conclusions

The available evidence suggests that medical treatment, with misoprostol, and expectant care are both acceptable alternatives to routine surgical evacuation given the availability of health service resources to support all three approaches. Further studies, including long-term follow-up, are clearly needed to confirm these findings. There is an urgent need for studies on women who miscarry at more than 13 weeks' gestation.

PLAIN LANGUAGE SUMMARY

Medical treatments for incomplete miscarriage

What is the issue?

Miscarriage is when a pregnant woman loses her baby before the baby would be considered able to survive outside the womb, i.e. before 24 weeks' gestation. Miscarriage occurs in about 10% to 15% of pregnancies and the signs are bleeding, usually with some abdominal pain and cramping. The traditional management of miscarriage was surgery but this Cochrane Review asks if medical treatments can be another management option for the woman.

Why is this important?

The cause of miscarriage is often unknown, but most are likely to be due to abnormalities in the baby's chromosomes. Women experiencing miscarriage may be quite distressed, and there can be feelings of emptiness, guilt, and failure. Fathers can also be affected emotionally. Traditionally, surgery (curettage or vacuum aspiration) has been the treatment used to remove any retained tissue and it is quick to perform. It has now been suggested that medical treatments (usually misoprostol) may be as effective and may carry less risk of infection.

What evidence did we find?

We searched for evidence on 13 May 2016 and identified 24 studies involving 5577 women, and all these studies were of women at less than 13 weeks' gestation. There were a number of different ways of giving the drugs and so there are limited data for each comparison.

Overall, the review found no real difference in the success between misoprostol and waiting for spontaneous miscarriage (expectant care), nor between misoprostol and surgery. The overall success rate of treatment (misoprostol and surgery) was over 80% and sometimes as high as 99%, and one study identified no difference in subsequent fertility between methods of medication, surgery or expectant management. Vaginal misoprostol was compared with oral misoprostol in one study which found no difference in success, but there was an increase in the incidence of diarrhoea with oral misoprostol. However, women on the whole seemed happy with their care, whichever treatment they were given.

What does this mean?

The review suggests that misoprostol or waiting for spontaneous expulsion of fragments are important alternatives to surgery, but women should be offered an informed choice. Further studies are clearly needed to confirm these findings and should include long-term follow-up. There is an urgent need for studies on women who miscarry at more than 13 weeks' gestation.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [Explanation]

Misoprostol compared to expectant care for incomplete miscarriage

Patient or population: incomplete miscarriage
Setting: hospitals in Australia, Sweden, United Kingdom
Intervention: misoprostol
Comparison: expectant care

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with expectant care	Risk with Misoprostol				
Complete miscarriage	Study population		RR 1.23 (0.72 to 2.10)	150 (2 RCTs)	⊕◯◯◯ VERY LOW [1,2,3]	
	579 per 1000	712 per 1000 (417 to 1000)				
	Moderate					
	687 per 1000	845 per 1000 (494 to 1000)				
Surgical evacuation	Study population		RR 0.62 (0.17 to 2.26)	308 (2 RCTs)	⊕⊕◯◯ LOW [12]	
	312 per 1000	193 per 1000 (53 to 704)				
	Moderate					
	327 per 1000	202 per 1000 (56 to 738)				
Unplanned surgical intervention	Study population		RR 0.62 (0.17 to 2.26)	308 (2 RCTs)	⊕⊕◯◯ LOW [12]	

	312 per 1000	193 per 1000 (53 to 704)				
	Moderate					
	327 per 1000	202 per 1000 (56 to 738)				
Women's views/ acceptability of method	Study population		-	(0 study)	-	No data
	see comment	see comment				
Nausea	Study population		-	(0 study)	-	No data
	see comment	see comment				
Vomiting	Study population		-	(0 study)	-	No data
	see comment	see comment				
Diarrhoea	Study population		-	(0 study)	-	No data
	see comment	see comment				

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).
CI: confidence interval; **RCT**: randomised controlled trial; **RR:** risk ratio.

GRADE Working Group grades of evidence
High-quality: We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate-quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low-quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Very low-quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1] One study blinded (placebo-controlled), but the other unblinded.
[2] High levels of heterogeneity.
[3] Only two trials, including a total of 150 women.

BACKGROUND

Description of the condition

Miscarriage is generally defined as the spontaneous loss of a pregnancy prior to 24 weeks' gestation, that is, before the fetus is usually viable outside the uterus (Shiers 2003). The clinical signs of miscarriage are vaginal bleeding, usually with abdominal pain and cramping. If the pregnancy has been expelled, the miscarriage is termed 'complete' or 'incomplete' depending on whether or not tissues are retained in the uterus. If a woman bleeds but her cervix is closed, this is described as a 'threatened miscarriage' as it is often possible for the pregnancy to continue and not to miscarry (RCOG 2006; Shiers 2003); if the pregnancy is in the uterus but the cervix is open, this is described as an 'inevitable miscarriage', i.e. it will not usually be possible to save the pregnancy and fetus. The now widespread use of ultrasound in early pregnancy, either for specific reasons (e.g. bleeding) or as a routine procedure, reveals pregnancies that are destined to inevitably miscarry, because they are 'non-viable' (Sawyer 2007; Weeks 2001). Non-viable pregnancies are either a 'missed miscarriage' if an embryo or fetus is present but is dead, or an 'anembryonic pregnancy' if no embryo has developed within the gestation sac.

Regardless of the type of miscarriage, the overall incidence is considered to be between 10% and 15%, although the real incidence may be greater (Shiers 2003). Most miscarriages occur within the first 12 weeks of pregnancy and are called 'early miscarriage', with those occurring after 13 weeks being known as 'late miscarriage'. The cause of miscarriage is generally unknown, but most are likely to be due to chromosomal abnormalities. The risk of miscarriage has been reported to be higher in older women, and where there are structural abnormalities of the genital tract, infection, and maternal complications such as diabetes, renal disease, and thyroid dysfunction. Also, some environmental factors have been linked with miscarriage, including alcohol and smoking (Shiers 2003). Miscarriage can sometimes lead to haemorrhage and infection, and it can be an important cause of morbidity, and even mortality, particularly in low-income countries (Lewis 2007).

Women experiencing miscarriage may be overwhelmed by the symptoms and also quite distressed (Shiers 2003). Psychological problems can follow a miscarriage, and these can include loss of self-esteem resulting from the woman's feeling of inability to rely on her body to give birth (Swanson 1999). Emotional responses described include those of emptiness, guilt, and failure (Swanson 1999). There can also be depression, anxiety, grief, and anger (Klier 2002; Thapar 1992). A number of other consequences, including sleep disturbance, social withdrawal, anger, and marital disturbance, may occur following miscarriage (Lok 2007). Fathers can also be affected emotionally (Klier 2002).

Description of the intervention

Traditionally, all pregnancies that had miscarried were considered by clinicians as potentially incomplete. Therefore, surgical curettage ('evacuation of the uterus') was performed routinely to remove any retained placental tissue. If no tissue was obtained, then a retrospective diagnosis of complete miscarriage was made. Surgical curettage was the 'gold standard management' for miscarriage for many years because it is quickly performed and it is possible to completely remove any retained products of conception (Ankum 2001). Histological examination of the removed tissues also allowed exclusion of trophoblastic disease, e.g. hydatidiform mole - although this is quite rare. New clinical approaches have evolved to try to minimise unnecessary surgical interventions whilst aiming to maintain low rates of morbidity and mortality from miscarriage. These approaches have included ultrasound imaging to diagnose complete miscarriage and thus avoid treatment, or more conservative treatments of incomplete miscarriage, such as drug (medical) treatment or no active treatment (expectant management) (Ankum 2001; Luise 2002). Various types of medical treatment could be suitable as alternatives to routine surgical treatment for miscarriage and these include the use of prostaglandins, or other uterotonic (uterus-contracting) drugs or anti-hormone therapy.

How the intervention might work

a) Prostaglandins, e.g. misoprostol, prostaglandin F2alpha

Misoprostol is a synthetic prostaglandin E1 analogue and is marketed for the prevention and treatment of peptic ulcers. Recognised as a potent method for pregnancy termination (Costa 1993; Norman 1991), it is inexpensive, stable at room temperature, and has few systemic effects, although vomiting, diarrhoea, hypertension, and even potential teratogenicity (causing fetal malformation) when misoprostol fails to induce the abortion, have been reported (Fonseca 1991).

Misoprostol has been shown to be an effective myometrial stimulant of the pregnant uterus, selectively binding to EP-2/EP-3 prostanoid receptors and stimulating contractions, which push the products or pregnancy out. It is rapidly absorbed orally and vaginally. Vaginally-absorbed serum levels are more prolonged, and vaginal misoprostol may have locally-mediated effects (Zieman 1997). Misoprostol could be especially useful in low-income countries, where transport and storage facilities are inadequate, and the availability of uterotonic agents and blood is limited. Its use in obstetrics and gynaecology has been explored, especially to induce first and second trimester abortion (Costa 1993; Norman 1991), for the induction of labour (Alfirevic 2014; Hofmeyr 2010), and for the prevention of postpartum haemorrhage (Tuncalp 2012). The stimulatory actions of misoprostol on the early pregnancy uterus could, in theory, help to expel retained tissue from the uterus

after miscarriage, and provide an attractive medical alternative to surgical treatment of incomplete miscarriage (Chung 1995). It is important to distinguish between the use of misoprostol for incomplete miscarriage and its use for termination of viable pregnancies.

b) Other uterotonics, e.g. ergometrine, oxytocin

Ergometrine (extracted from the rye fungus, ergot) will promote contraction of involuntary muscles throughout the body (Hawk 1985; Kawarabayashi 1990), and oxytocin promotes strong rhythmic contractions of the uterus (Arthur 2007; Mota-Rojas 2007). Both drugs could potentially have a role in expelling tissue after miscarriage.

c) Progesterone antagonist

A number of progesterone antagonists are now available, and these drugs will interfere with the production, or functioning, or both, of progesterone. The progesterone antagonist, mifepristone, has an established role in the termination of first and second trimester pregnancy (Jain 2002), and may also be effective in promoting expulsion of retained placental tissues following miscarriage (Tang 2006b).

Why it is important to do this review

Bleeding in early pregnancy is the most common reason for women to present to the gynaecology emergency department, and in many of these women, miscarriage will be diagnosed (Ramphal 2006). It is now clear that routine surgical evacuation of the uterus following miscarriage may not be indicated, and the subsequent risk of infection, haemorrhage, cervical damage, uterine perforation, and risks of anaesthesia may not be justified (Harris 2007). In order to optimise clinical management of this common condition, it is important to establish whether the use of medical treatment (drugs), or expectant management (no routine treatment) may offer a safer alternative for women with incomplete miscarriage, and whether there are specific circumstances where one type of treatment plan is superior to others.

We initially aimed to systematically review medical treatments for both non-viable pregnancies and incomplete miscarriages combined. On further reflection, this seemed illogical. Non-viable pregnancies contain viable trophoblast (placental) tissue, which produces hormones, which may in theory make these pregnancies more susceptible to anti-hormone therapy and more resistant to uterotonic (stimulating uterine contractions) therapy than pregnancies in which (incomplete) miscarriage has already taken place. Therefore, this review focuses on the management of incomplete miscarriage. Another Cochrane Review has covered non-viable pregnancies (Neilson 2006).

Other relevant Cochrane Reviews on the treatment of miscarriage include: '*Expectant care versus surgical treatment for miscarriage*' (Nanda 2012), '*Surgical procedures for evacuating incomplete miscarriage*' (Tuncalp 2010), '*Anaesthesia for evacuation of incomplete miscarriage*' (Calvache 2012), and '*Follow-up for improving psychological well being for women after a miscarriage*' (Murphy 2012). There is also a series of Cochrane Reviews on the possible prevention of miscarriage (Aleman 2005; Bamigboye 2003; Empson 2005; Haas 2013; de Jong PG 2014; Wong 2014; Balogun 2016). In addition, there are Cochrane Reviews on medical and surgical interventions for induced abortions (Dodd 2010; Kulier 2011; Lohr 2008; Wildschut 2011; Say 2010).

OBJECTIVES

To assess the effectiveness, safety, and acceptability of any medical treatment for incomplete miscarriage (before 24 weeks).

METHODS

Criteria for considering studies for this review

Types of studies

We only included randomised controlled trials (RCTs). Cluster-randomised trials were eligible for inclusion, although we did not identify such trials. We excluded quasi-RCTs and cross-over trials. We also excluded conference proceedings and abstracts.

Types of participants

Participants were women being treated for spontaneous miscarriage (pregnancy loss at less than 24 weeks), either where there was ultrasound evidence of retained tissue (incomplete miscarriage) or where the diagnosis had been made on clinical grounds alone, and where there would be uncertainty whether the miscarriage was complete or incomplete. In communities in which termination of pregnancy was illegal or unavailable, this could have included women who had undergone unsafe abortion.

We excluded women with non-viable pregnancies (i.e. where the embryo or fetus had died in utero, but in whom miscarriage had not yet occurred) as they are covered by another Cochrane Review (Neilson 2006).

We also excluded studies on induced abortion of a live fetus and for fetal anomaly as these are covered in other Cochrane Reviews (Dodd 2010; Kulier 2011; Lohr 2008; Wildschut 2011; Say 2010).

Types of interventions

We considered trials if they compared medical treatment of incomplete miscarriage with other methods (e.g. expectant management, placebo, or any other intervention including surgical evacuation, either curettage or vacuum aspiration). We also included comparisons between different routes of administration of drugs (e.g. oral versus vaginal), or between different drugs or doses of drug, or duration or timing of treatment, if data existed.

Types of outcome measures

Primary outcomes

1. Complete miscarriage (diagnosis of complete miscarriage based on findings at surgery, or ultrasound examination, or both, after a specific period, or cessation of symptoms and signs, or both).
2. Surgical evacuation.
3. Death or serious complications (e.g. uterine rupture, haemorrhage, sepsis, coagulopathy, uterine perforation, hysterectomy, organ failure, intensive care unit admission).

Secondary outcomes

1. Unplanned surgical intervention (i.e. a second evacuation in the surgical group but a first evacuation in the medical or expectant group).
2. Blood transfusion.
3. Haemorrhage (blood loss greater than 500 mL, or as defined by trial authors).
4. Blood loss.
5. Anaemia (haemoglobin (Hb) less than 10 g/dL, or as defined by trial authors).
6. Days of bleeding.
7. Pain relief.
8. Pelvic infection.
9. Cervical damage.
10. Digestive disorders (nausea or vomiting or diarrhoea).
11. Hypertensive disorders.
12. Duration of stay in hospital.
13. Psychological effects.
14. Subsequent fertility.
15. Women's views/acceptability of method.
16. Pathology of fetal/placental tissue.
17. Costs.

Search methods for identification of studies

The following methods section of this review is based on a standard template used by Cochrane Pregnancy and Childbirth.

Electronic searches

The Information Specialist searched Cochrane Pregnancy and Childbirth's Trials Register on 13 May 2016.

The Register is a database containing over 22,000 reports of controlled trials in the field of pregnancy and childbirth. For full search methods used to populate Pregnancy and Childbirth's Trials Register, including the detailed search strategies for CENTRAL, MEDLINE, Embase, and CINAHL, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service, please follow this link to the editorial information about Cochrane Pregnancy and Childbirth in the Cochrane Library and select the '*Specialized Register*' section from the options on the left side of the screen.

Briefly, Cochrane Pregnancy and Childbirth's Trials Register is maintained by their Information Specialist and contains trials identified from:

1. monthly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
2. weekly searches of MEDLINE (Ovid);
3. weekly searches of Embase (Ovid);
4. monthly searches of CINAHL (EBSCO);
5. handsearches of 30 journals and the proceedings of major conferences;
6. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Search results are screened by two people and the full-text of all relevant trial reports identified through the searching activities described above is reviewed. Based on the intervention described, each trial report is assigned a number that corresponds to a specific Pregnancy and Childbirth review topic (or topics), and is then added to the Register. The Information Specialist searches the Register for each review using this topic number rather than keywords. This results in a more specific search set which has been fully accounted for in the relevant review sections (Included studies; Excluded studies; Ongoing studies).

Searching other resources

We searched reference lists at the end of papers for further studies. We did not apply any language or date restrictions.

Data collection and analysis

For methods used in the previous version of this review, see Neilson 2013.

For this update, we used the following methods for assessing the 21 reports that we identified as a result of the updated search.

The following Methods section of this review is based on a standard template used by Cochrane Pregnancy and Childbirth.

Selection of studies

Two review authors (CRK, SB) independently assessed for inclusion all the potential studies we identified as a result of the search strategy. We would have resolved any disagreement through discussion or, if had been required, through consultation with a third person.

Data extraction and management

We designed a form to extract data. For eligible studies, two review authors (CRK, SB) extracted the data using the agreed form. We would have resolved any disagreement through discussion or, if had been required, through consultation with a third person. We entered data into Review Manager 5 software (RevMan 2014), and checked for accuracy.

Had any information regarding any of the above been unclear, we would have attempted to contact authors of the original reports to provide further details.

Assessment of risk of bias in included studies

Two review authors (CRK SB) independently assessed risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We would have resolved any disagreement through discussion or, if had been required, through consultation with a third person.

(1) Random sequence generation (checking for possible selection bias)

We have described for each included study the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.

We have assessed the methods as:

- low risk of bias (any truly random process, e.g. random number table; computer random number generator);
- high risk of bias (any non-random process, e.g. odd or even date of birth; hospital or clinic record number);
- unclear risk of bias.

(2) Allocation concealment (checking for possible selection bias)

We described for each included study the method used to conceal allocation to interventions prior to assignment and assessed whether intervention allocation could have been foreseen in advance of, or during recruitment, or changed after assignment.

We assessed the methods as:

- low risk of bias (e.g. telephone or central randomisation; consecutively numbered sealed opaque envelopes);
- high risk of bias (open random allocation; unsealed or non-opaque envelopes, alternation; date of birth);
- unclear risk of bias.

(3.1) Blinding of participants and personnel (checking for possible performance bias)

We described for each included study the methods used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. We considered that studies were at low risk of bias if they were blinded, or if we judged that the lack of blinding was unlikely to affect results. We assessed blinding separately for different outcomes or classes of outcomes.

We assessed the methods as:

- low, high, or unclear risk of bias for participants;
- low, high, or unclear risk of bias for personnel.

(3.2) Blinding of outcome assessment (checking for possible detection bias)

We described for each included study the methods used, if any, to blind outcome assessors from knowledge of which intervention a participant received. We assessed blinding separately for different outcomes or classes of outcomes.

We assessed methods used to blind outcome assessment as:

- low, high, or unclear risk of bias.

(4) Incomplete outcome data (checking for possible attrition bias due to the amount, nature, and handling of incomplete outcome data)

We described for each included study, and for each outcome or class of outcomes, the completeness of data, including attrition and exclusions from the analysis. We stated whether attrition and exclusions were reported and the numbers included in the analysis at each stage (compared with the total randomised participants), reasons for attrition or exclusion, where reported, and whether missing data were balanced across groups or were related to outcomes. Where sufficient information was reported, or could be supplied by the trial authors, we planned to re-include missing data in the analyses which we undertook.

We assessed methods as:

- low risk of bias (e.g. no missing outcome data; missing outcome data balanced across groups);
- high risk of bias (e.g. numbers or reasons for missing data imbalanced across groups; 'as treated' analysis done with substantial departure of intervention received from that assigned at randomisation);
- unclear risk of bias.

(5) Selective reporting (checking for reporting bias)

We described for each included study how we investigated the possibility of selective outcome reporting bias and what we found.

We assessed the methods as:

- low risk of bias (where it is clear that all of the study's prespecified outcomes and all expected outcomes of interest to the review have been reported);

- high risk of bias (where not all the study's prespecified outcomes have been reported; one or more reported primary outcomes were not prespecified; outcomes of interest are reported incompletely and so cannot be used; study fails to include results of a key outcome that would have been expected to have been reported);
- unclear risk of bias.

(6) Other bias (checking for bias due to problems not covered by (1) to (5) above)

We described for each included study any important concerns we had about other possible sources of bias.

(7) Overall risk of bias

We made explicit judgements about whether studies were at high risk of bias, according to the criteria given in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). With reference to (1) to (6) above, we planned to assess the likely magnitude and direction of the bias and whether we considered it is likely to impact on the findings. In future updates, we will explore the impact of the level of bias through undertaking sensitivity analyses - see Sensitivity analysis.

Assessment of the quality of the evidence using the GRADE approach

For this update, we assessed the quality of the evidence using the GRADE approach as outlined in the GRADE Handbook in order to assess the quality of the body of evidence relating to the following outcomes for the two main comparisons: misoprostol versus expectant care and misoprostol versus surgery.

1. Complete miscarriage
2. Surgical evacuation
3. Unplanned surgical intervention
4. Women's views/acceptability of method (for misoprostol versus surgery only)
5. Nausea
6. Vomiting
7. Diarrhoea

We used GRADEpro Guideline Development Tool to import data from Review Manager 5 in order to create 'Summary of findings' tables (RevMan 2014). We produced a summary of the intervention effect and a measure of quality for each of the above outcomes using the GRADE approach. The GRADE approach uses five considerations (study limitations, consistency of effect, imprecision, indirectness, and publication bias) to assess the quality of the body of evidence for each outcome. The evidence can be downgraded from 'high-quality' by one level for serious (or by two levels for very serious) limitations, depending on assessments for risk of bias, indirectness of evidence, serious inconsistency, imprecision of effect estimates, or potential publication bias.

Measures of treatment effect

Dichotomous data

For dichotomous data, we presented results as summary risk ratios (RRs) with 95% confidence intervals (CIs).

Continuous data

For continuous data, we used the mean difference (MD) if outcomes were measured in the same way between trials. We used the standardised mean difference (SMD) to combine trials that measured the same outcome, but used different methods.

Unit of analysis issues

Cluster-randomised trials

We planned to include cluster-randomised trials in the analyses along with individually-randomised trials, however, we did not identify any cluster-randomised trials. If we identify any such trials in future updates, we will adjust their sample sizes using the methods described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Section 16.3.4) using an estimate of the intracluster correlation coefficient (ICC) derived from the trial (if possible), from a similar trial or from a study of a similar population (Higgins 2011). If we use ICCs from other sources, we will report this and conduct sensitivity analyses to investigate the effect of variation in the ICC. If we identify both cluster-randomised trials and individually-randomised trials, we plan to synthesise the relevant information. We will consider it reasonable to combine the results from both if there is little heterogeneity between the study designs and the interaction between the effect of intervention and the choice of randomisation unit is considered to be unlikely. We will also acknowledge heterogeneity in the randomisation unit and perform a sensitivity analysis to investigate the effects of the randomisation unit.

Cross-over trials

These are considered inappropriate studies for this review.

Dealing with missing data

For included studies, we noted levels of attrition. In future updates, if we include more eligible studies, we will explore the impact of including studies with high levels of missing data in the overall assessment of treatment effect by using sensitivity analysis.

For all outcomes, we carried out analyses, as far as possible, on an intention-to-treat basis, i.e. we attempted to include all participants randomised to each group in the analyses. The denominator for each outcome in each trial was the number randomised minus any participants whose outcomes were known to be missing.

Assessment of heterogeneity

We assessed statistical heterogeneity in each meta-analysis using the Tau², I², and Chi² statistics. We regarded heterogeneity as substantial if I² was greater than 30% and either Tau² was greater than zero, or there was a low P value (less than 0.10) in the Chi² test for heterogeneity. If we identified substantial heterogeneity (above 30%), we planned to explore it by prespecified subgroup analysis.

Assessment of reporting biases

With this update, there were several outcomes in the meta-analysis that included 10 or more studies. Therefore, we investigated reporting biases (such as publication bias). We assessed funnel plot asymmetry visually.

Data synthesis

We carried out statistical analysis using the Review Manager 5 software (RevMan 2014). We used a fixed-effect meta-analysis for combining data where it was reasonable to assume that studies were estimating the same underlying treatment effect, i.e. where trials were examining the same intervention, and the trials' populations and methods were judged sufficiently similar.

If there was clinical heterogeneity sufficient to expect that the underlying treatment effects differed between trials, or if we detected substantial statistical heterogeneity, we used a random-effects meta-analysis to produce an overall summary if we considered an average treatment effect across trials to be clinically meaningful. We treated the random-effects summary as the average of the range of possible treatment effects and we discuss the clinical implications of treatment effects differing between trials. If the average treatment effect was not clinically meaningful, we planned not to combine trials. If we used random-effects analyses, we presented the results as the average treatment effect with 95% CIs, and the estimates of Tau² and I².

Subgroup analysis and investigation of heterogeneity

When we identified substantial heterogeneity, we investigated it using subgroup analyses and sensitivity analyses. We considered whether an overall summary was meaningful, and if it was, used random-effects analysis to produce it.

For misoprostol versus expectant care, and misoprostol versus surgery, we subgrouped studies by the route of administration of misoprostol (vaginal, oral, sublingual, rectal, combined).

For the remaining comparisons, we carried out the following subgroup analyses on all outcomes.

1. Women less than 13 weeks' gestation versus women between 13 and 23 weeks' gestation versus gestation not specified.

We assessed subgroup differences by interaction tests available within Review Manager 5 (RevMan 2014). We reported the results of subgroup analyses quoting the Chi² statistic and P value, and the interaction test I² value.

Sensitivity analysis

We planned to carry out sensitivity analyses to explore the effect of trial quality assessed by concealment of allocation, high attrition rates, or both, with poor quality studies being excluded from the analyses in order to assess whether this makes any difference to the overall result. We did not carry this out due to lack of data in separate comparisons.

RESULTS

Description of studies

See Characteristics of included studies; Characteristics of excluded studies; Characteristics of ongoing studies.

Results of the search

We identified 164 reports in the original search (September 2009) that covered medical interventions for miscarriage before 24 weeks' gestation, both for women with incomplete miscarriage and women with intrauterine fetal death. We identified 30 reports from an updated search on 23 July 2012. We identified 21 reports from an updated search on 13 May 2016.

We included 24 trials, involving 5577 women in the review (Bique 2007; Blanchard 2004; Blohm 2005; Chigbu 2012; Clevin 2001; Dabash 2010; Dao 2007; Diop 2009; Ganguly 2010; Montesinos 2011; Moodliar 2005; Ngoc 2005; Niinimaki 2006; Pang 2001; Paritakul 2010; Patua 2013; Sahin 2001; Shelley 2005; Shochet 2012; Shwekerela 2007; Taylor 2011; Trinder 2006; Weeks 2005; Zhang 2005); and two trials are ongoing (ISRCTN65305620; NCT01033903). We excluded the remaining trials (reasons listed in table of Characteristics of excluded studies).

Included studies

Twenty of the 24 included studies involved only women with incomplete miscarriage (Bique 2007; Blanchard 2004; Blohm 2005; Chigbu 2012; Clevin 2001; Dabash 2010; Dao 2007; Diop 2009; Montesinos 2011; Moodliar 2005; Ngoc 2005; Pang 2001; Paritakul 2010; Patua 2013; Sahin 2001; Shelley 2005; Shochet 2012; Shwekerela 2007; Taylor 2011; Weeks 2005). Seventeen of the studies took place in low-income countries, mainly in Africa and Southeast Asia. Three studies included both women with incomplete miscarriage and women with an intrauterine fetal death (Niinimaki 2006; Trinder 2006; Zhang 2005). One of these studies reported the findings for incomplete miscarriage separately

from those for intrauterine fetal death (Trinder 2006), and for the other two studies, the authors kindly sent us the separated data (Niinimaki 2006; Zhang 2005). One study included women with early pregnancy failure, which encompassed the anembryonic gestation, embryonic or fetal death, inevitable miscarriage, and incomplete miscarriage (Ganguly 2010). This study reported the findings for incomplete miscarriage separately from the other pregnancy failure types for the primary outcome. There are a further 12 studies that recruited both women with incomplete miscarriage and women with intrauterine fetal death, and we have tried to contact these authors for the separated data, but as yet have been unsuccessful. We have therefore excluded these studies from this review.

All of the 24 included trials addressed medical treatment for incomplete miscarriage before 13 weeks and we found no relevant studies addressing this question for women between 13 and 23 weeks' gestation.

Fourteen of the studies used ultrasound to confirm the diagnosis (Blanchard 2004; Blohm 2005; Clevin 2001; Dao 2007; Ganguly 2010; Montesinos 2011; Moodliar 2005; Ngoc 2005; Niinimaki 2006; Pang 2001; Paritakul 2010; Patua 2013; Zhang 2005). The other studies used clinical assessment for the diagnosis (Bique 2007; Chigbu 2012; Shelley 2005; Shwekerela 2007; Trinder 2006; Weeks 2005), or clinical examination supplemented by ultrasound, when necessary (Dabash 2010; Diop 2009; Shochet 2012; Taylor 2011). The trials assessed completeness of miscarriage at follow-up, either by ultrasound or clinical assessment, and at times that varied from three days to eight weeks. We have included the specific information in the Characteristics of included studies and also at the beginning of the 'Results' section for each comparison.

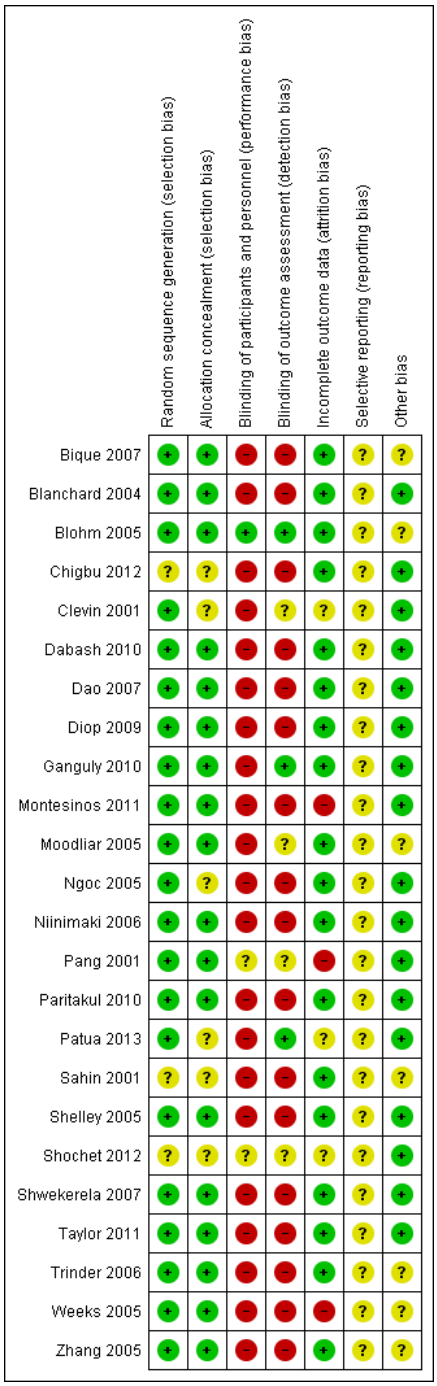
Excluded studies

There are 148 excluded studies and these are listed in the reference section under 'Excluded studies'. The table Characteristics of excluded studies states the reasons for exclusion from this review. These reasons mainly include: study not randomised; study including women with non-viable pregnancies or intrauterine fetal death only; and studies including women having termination of pregnancy. We have also excluded studies where we have been unable to contact the authors for data separated by incomplete miscarriage and intrauterine fetal death (Bagratee 2004; Demetroulis 2001; Hinshaw 1997; Johnson 1997; Louey 2000 [pers comm]; Machtinger 2004; Ngai 2001; Nielsen 1999; Shaikh 2008). Where authors have kindly responded, but have been unable to supply their data separated by incomplete miscarriage and intrauterine fetal death, we have also been compelled to exclude such studies (Chung 1999; Kong 2013; Petersen 2013).

Risk of bias in included studies

Overall, the risk of bias of studies was generally low, although in most studies it was not possible to blind participants and clinicians. It was unclear whether any of the studies were free of selective reporting bias as we did not assess the trial protocols (Figure 1).

Figure 1. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.



Allocation

We excluded studies where group allocation was not random. We considered the random sequence generation to be at low risk of bias in all studies except three (Chigbu 2012; Sahin 2001; Shochet 2012), where it was unclear. We considered allocation concealment to be at low risk of bias in all studies except six (Chigbu 2012; Clevin 2001; Ngoc 2005; Patua 2013; Sahin 2001; Shochet 2012), where it was unclear.

Blinding

We considered blinding to be at low risk of performance bias in only one study (Blohm 2005), and low risk for detection bias in three studies (Blohm 2005; Ganguly 2010; Patua 2013). There was unclear risk of performance bias in two studies (Pang 2001; Shochet 2012), and for detection bias it was unclear in four studies (Clevin 2001; Moodliar 2005; Pang 2001; Shochet 2012). For the remainder of the studies, we considered blinding to be at high risk of bias. However, for many studies we considered it impossible to blind, especially where medical treatment was being compared with surgery.

Incomplete outcome data

Loss to follow-up and exclusions after randomisation were low in all studies except six; for three, we considered them unclear (Clevin 2001; Patua 2013; Shochet 2012), and another three, we considered to be at high risk of bias (Montesinos 2011; Pang 2001; Weeks 2005). In the Montesinos 2011 study, 16.1% of women did not return for assessment and were not included in analyses. In the Pang 2001 study, it appeared that intention-to-treat analysis was not used and the data could not be re-included. In the Weeks 2005 study, there was complete follow-up at six days, but by two weeks there was a 33% loss to follow-up in the misoprostol group and 45% in the group having surgery. This was explained by women not returning from their communities for follow-up.

Selective reporting

It was unclear to us whether any of the studies were free of selective reporting bias as we were unable to assess the protocols for the studies.

Other potential sources of bias

Seventeen out of the 24 studies appeared to be free of other sources of bias (Blanchard 2004; Chigbu 2012; Clevin 2001; Dabash 2010; Dao 2007; Diop 2009; Ganguly 2010; Montesinos 2011; Ngoc 2005; Niinimaki 2006; Pang 2001; Paritakul 2010; Patua 2013; Shelley 2005; Shochet 2012; Shwekerela 2007; Taylor 2011), and for the remainder, it was unclear.

Effects of interventions

See: **Summary of findings for the main comparison** Misoprostol compared to expectant care for incomplete miscarriage; **Summary of findings 2** Misoprostol compared to surgery for incomplete miscarriage

All 24 studies assessed the medical treatment of incomplete miscarriage for women at less than 13 weeks' gestation. There were no studies involving women between 13 and 23 weeks' gestation, and none where gestation was not specified.

For the comparisons of misoprostol (by any route of administration versus expectant care or versus surgery), we used random-effects meta-analyses because of the clinical heterogeneity around route of administration. For other meta-analyses, we used the fixed-effect model, except where significant heterogeneity was indicated (see Assessment of heterogeneity above). Please note we did not conduct any subgroup analyses on gestation for all comparisons due to lack of data.

1. Misoprostol versus expectant care (3 studies, 335 women, Analyses 1.1 to 1.7)

For women less than 13 weeks' gestation

Three studies involving 335 women addressed this comparison for women with incomplete miscarriage (Blohm 2005; Shelley 2005; Trinder 2006). There were two further studies that involved both women with incomplete miscarriage and women with intrauterine fetal deaths, but to date we have been unable to obtain the data separated by incomplete miscarriage and intrauterine fetal death for these studies (Bagratee 2004; Ngai 2001).

Diagnosis of incomplete miscarriage and assessment of complete miscarriage after treatment were made using clinical judgement in two studies (Shelley 2005; Trinder 2006), and using ultrasound in one study (Blohm 2005). Assessment of the outcome of complete miscarriage was made at differing times in the three studies: Blohm 2005 assessed at one week and Shelley 2005 at 10 to 14 days. As Trinder 2006 assessed at eight weeks, we have not included these data (there was an assessment at two weeks, but the findings were not reported separately for women with incomplete miscarriage and women with intrauterine fetal death). We have written to the authors to seek these data.

All the studies looked at vaginal misoprostol compared with expectant care (Blohm 2005; Shelley 2005; Trinder 2006). There were no studies assessing other routes of administration.

The studies are at low risk of bias overall. However, blinding of participants and clinicians was only used in one (Blohm 2005).
We chose to use random-effects meta-analyses for all the outcomes in this comparison as we believe there is clinical heterogeneity as we will be potentially pooling differing routes of administration (vaginal, oral, rectal, and sublingual). We have therefore, reported the average risk ratio (RR) or mean difference (MD). Although there are currently only data from studies using vaginal misoprostol, we believe other studies will be undertaken in the future and will be added at future updates to this review. We have assessed the individual routes of administration of misoprostol for effectiveness (below, in Comparisons 3 to Comparison 8).

Primary outcomes

Complete miscarriage

Only two of the three studies assessed this outcome (Blohm 2005; Shelley 2005), with the primary outcome for the third study being infection at 14 days (Trinder 2006). We rated the quality of the evidence as very low (Summary of findings for the main comparison), mainly due to high levels of heterogeneity, a small number of women involved (n = 150), and only one of the two studies being blinded.
There was no difference identified in complete miscarriage between misoprostol and expectant care (average risk ratio (RR) 1.23, 95% confidence interval (CI) 0.72 to 2.10; 2 studies, 150 women, random-effects (Tau^2 = 0.12; Chi^2 P = 0.02; I^2 = 81%)) (Analysis 1.1, very low-quality evidence). In terms of clinical impact, the success rate with misoprostol ranged from 80% to 81% and for expectant care from 52% to 85%. The heterogeneity may result from the different times at which complete miscarriage was assessed with expectant care. One study assessed at one week and found a success rate of 52% (Blohm 2005); the other study assessed at two weeks and found a success rate of 85% (Shelley 2005).

Surgical evacuation

We rated the quality of the evidence as low (Summary of findings for the main comparison), mainly due to high levels of heterogeneity and only one of the two studies being blinded. We also did not identify a difference in the need for surgical evacuation between misoprostol and expectant care (average RR 0.62, 95% CI 0.17 to 2.26; 2 studies, 308 women, random-effects (Tau^2 = 0.78; Chi^2 P = 0.003; I^2 = 89%)) (Analysis 1.2, low-quality evidence).

Death or serious complication

The outcome of death or serious complication showed no difference either (RR 2.91, 95% CI 0.12 to 70.05; 1 study, 126 women) (Analysis 1.3), although the review is underpowered to assess this outcome.

Secondary outcomes

Unplanned surgical intervention

We rated the quality of the evidence as low (Summary of findings for the main comparison), mainly due to high levels of heterogeneity and only one of the two studies being blinded. We did not identify a difference in unplanned surgical intervention between misoprostol and expectant care (average RR 0.62, 95% CI 0.17 to 2.26; 2 studies, 308 women, random-effects (Tau^2 = 0.78; Chi^2 P = 0.003; I^2 = 89%)) (Analysis 1.4, low-quality evidence).

Blood transfusion

We did not identify a difference in the number of blood transfusions undertaken (RR 3.07, 95% CI 0.13 to 74.28; 3 studies, 332 women), although only one study was estimable (Analysis 1.5).
Haemorrhage
There was no information reported on haemorrhage.
Blood loss
There was no information reported on blood loss.
Anaemia
There was no information reported on anaemia.
Days of bleeding
There was no information reported on days of bleeding.

Pain relief

We did not identify a difference in pain relief (average RR 1.12, 95% CI 0.67 to 1.88; 2 studies, 308 women, random-effects (Tau^2 = 0.10; Chi^2 P = 0.08; I^2 = 67%)) (Analysis 1.6).

Pelvic infection

We did not identify a difference in pelvic infection (average RR 2.42, 95% CI 0.59 to 9.98; 3 studies, 333 women, random-effects (Tau^2 = 0.00; Chi^2 P = 0.43, I^2 = 0%)) (Analysis 1.7).
Cervical damage
There was no information reported on cervical damage.
Digestive disorders (including nausea, vomiting, diarrhoea)
There was no information reported on digestive disorders.
Hypertensive disorders
There was no information reported on hypertensive disorders.

Duration of stay in hospital

There was no information reported on duration of stay in the hospital.

Psychological effects

There was no information reported on psychological effects.

Subsequent fertility

There was no information reported on subsequent fertility.

Women's views/acceptability of method

There was no information reported on women's views.

Pathology of fetal/placental tissue

There was no information reported on pathology of fetal/placental tissue.

Costs

There was no information reported on costs.

2. Misoprostol versus surgery (16 studies, 4044 women, Analyses 2.1 to 2.17)

For women less than 13 weeks' gestation

Sixteen studies involving 4044 women addressed this comparison for women with incomplete miscarriage at less than 13 weeks' gestation (Bique 2007; Chigbu 2012; Dabash 2010; Dao 2007; Ganguly 2010; Montesinos 2011; Moodliar 2005; Patua 2013; Sahin 2001; Shelley 2005; Shochet 2012; Shwekerela 2007; Taylor 2011; Trinder 2006; Weeks 2005; Zhang 2005). One of these studies was a comparison of misoprostol versus surgery versus expectant management (Trinder 2006), and therefore the comparison is described in the appropriate sections (here and the prior Section 1. Misoprostol versus expectant management).

The included studies were of low risk of bias overall (Figure 1), with most having adequate sequence generation and concealment allocation, although for Sahin 2001 and Shochet 2012, it was unclear. Blinding was not possible in any of the studies when comparing medical treatment with surgery. Only two studies had incomplete data and both related to the study being undertaken in rural settings where women in the community did not return for follow-up checks (Montesinos 2011; Weeks 2005). We were unclear about the possibility of selective reporting bias as we did not assess any of the study protocols. Six of the 12 studies appeared to be free of other biases (Dabash 2010; Dao 2007; Montesinos 2011; Shelley 2005; Shwekerela 2007; Taylor 2011).

Diagnosis of incomplete miscarriage and assessment of complete miscarriage after treatment was made using clinical judgement in five studies (Bique 2007; Chigbu 2012; Shelley 2005; Shwekerela 2007; Weeks 2005), using ultrasound in eight studies (Dabash 2010; Dao 2007; Ganguly 2010; Montesinos 2011; Moodliar 2005; Patua 2013; Sahin 2001; Zhang 2005), and other studies sometimes used ultrasound. Assessment of the outcome of complete miscarriage was made at differing times in the studies: one study assessed 24 hours after the last dose of misoprostol or the surgical evacuation (Patua 2013), 11 studies assessed at one week (Bique 2007; Chigbu 2012; Dabash 2010; Dao 2007; Ganguly 2010; Montesinos 2011; Shochet 2012; Shwekerela 2007; Taylor 2011; Weeks 2005; Zhang 2005), and three studies assessed around 10 to 14 days (Moodliar 2005; Sahin 2001; Shelley 2005). Trinder 2006 assessed at eight weeks and so we have not included these data (there was an assessment at two weeks in this study, but the findings were not reported separately for women with incomplete miscarriage and women with intrauterine fetal death). We have written to the authors to seek these data.

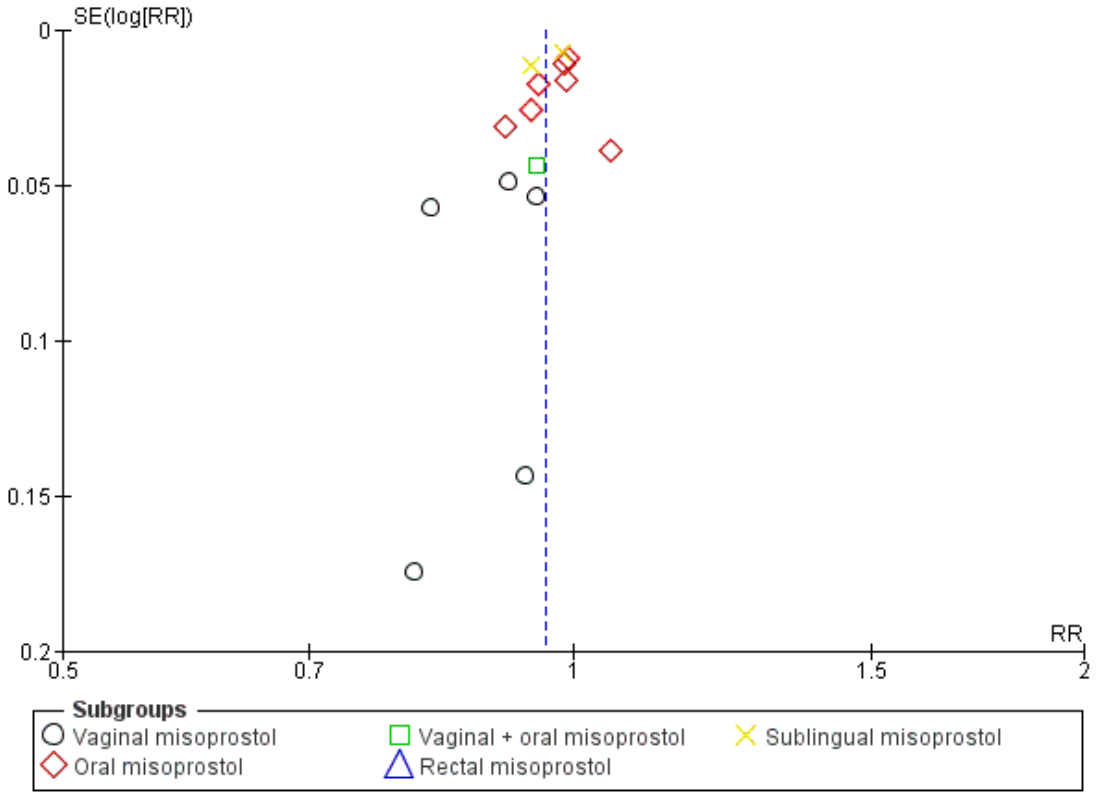
We have chosen to use random-effects meta-analyses for all the outcomes in this comparison as we believe there is clinical heterogeneity as we will be potentially pooling differing routes of administration (vaginal, oral, vaginal + oral, rectal, and sublingual). Although there are currently only data from studies using vaginal misoprostol, we believe other studies will be undertaken in the future and will be added to future updates of this review. We have assessed the individual routes of administration of misoprostol for effectiveness compared with surgery below in Comparisons 7 to 11.

Primary outcomes

Complete miscarriage

We rated the quality of the evidence as very low (Summary of findings 2), mainly due to high heterogeneity, the trials being inevitably unblinded, and suspicion of publication bias. There appeared to be fewer complete miscarriages with misoprostol compared with surgery (average RR 0.96, 95% CI 0.94 to 0.98, 15 studies; 3862 women, random-effects (Tau^2 = 0.00; Chi^2 P < 0.00001, I^2 = 73%)) (Analysis 2.1), although the upper CI was at 0.98. The funnel plot suggests there could be some missing studies or that there is a lack of smaller studies demonstrating a RR greater than one, so the findings need to be interpreted with caution (Figure 2). However, from the clinical perspective, the success rate was very good for both misoprostol and surgery. Misoprostol achieving between 80% and 99% success across studies, and surgery achieving between 91% and 100% success across studies. The interaction test identified no difference between the subgroups of differing routes of misoprostol administration compared with surgery for this outcome (interaction test (IT) P = 0.08, I^2 = 56.1%) (Analysis 2.1).

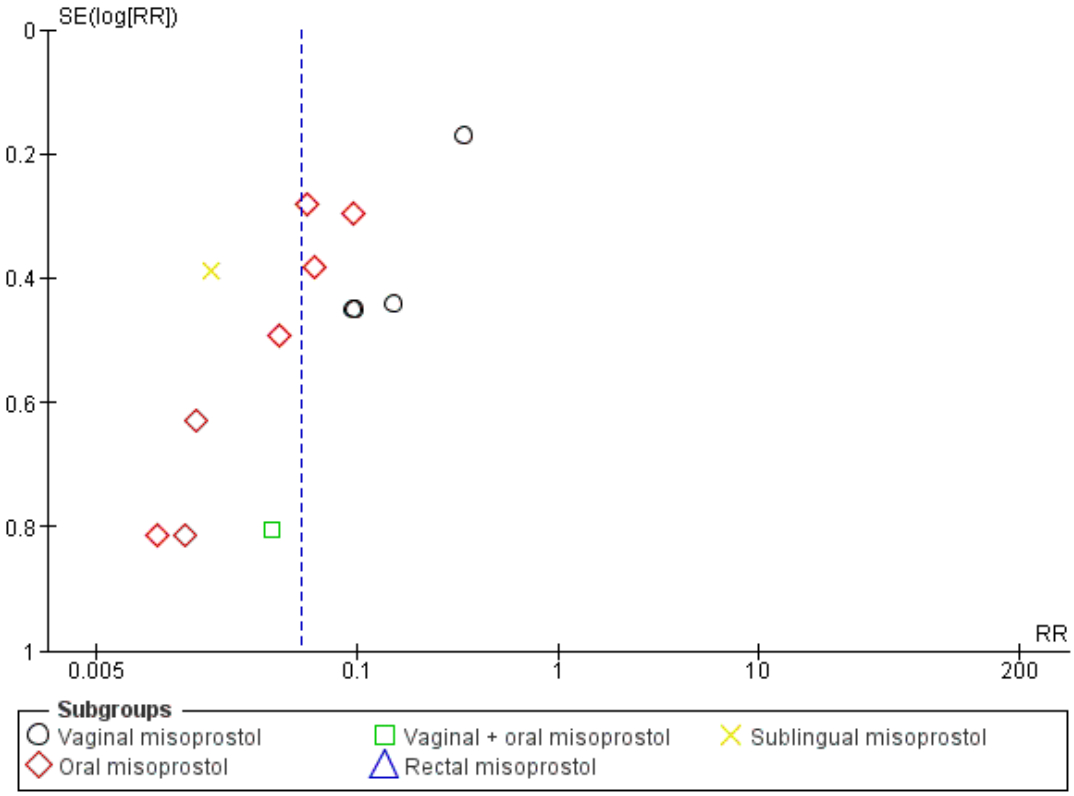
Figure 2. Funnel plot of comparison: 2 Misoprostol versus surgery, outcome: 2.1 Complete miscarriage.



Surgical evacuation

We rated the quality of the evidence as very low (Summary of findings 2), due to high heterogeneity, the trials being inevitably unblinded, and the possibility of publication bias. There were fewer surgical evacuations with misoprostol (average RR 0.05, 95% CI 0.02 to 0.11; 13 studies, 3070 women, random-effects (Tau^2 = 1.64; Chi^2 P < 0.00001; I^2 = 92%)) (Analysis 2.2). The funnel plot is asymmetrical, suggesting that smaller studies of lower methodological quality are showing an exaggerated effect size (Figure 3). The interaction test suggested there may be differences between the subgroups of differing routes of misoprostol administration compared with surgery for this outcome (IT P = 0.002, I^2 = 79.8%) (Analysis 2.2). However, many of the subgroups have little or no data, and when comparing just the two main subgroups (oral misoprostol and vaginal misoprostol), there is no longer any subgroup difference.

Figure 3. Funnel plot of comparison: 2 Misoprostol versus surgery, outcome: 2.2 Surgical evacuation.



Death or serious complication

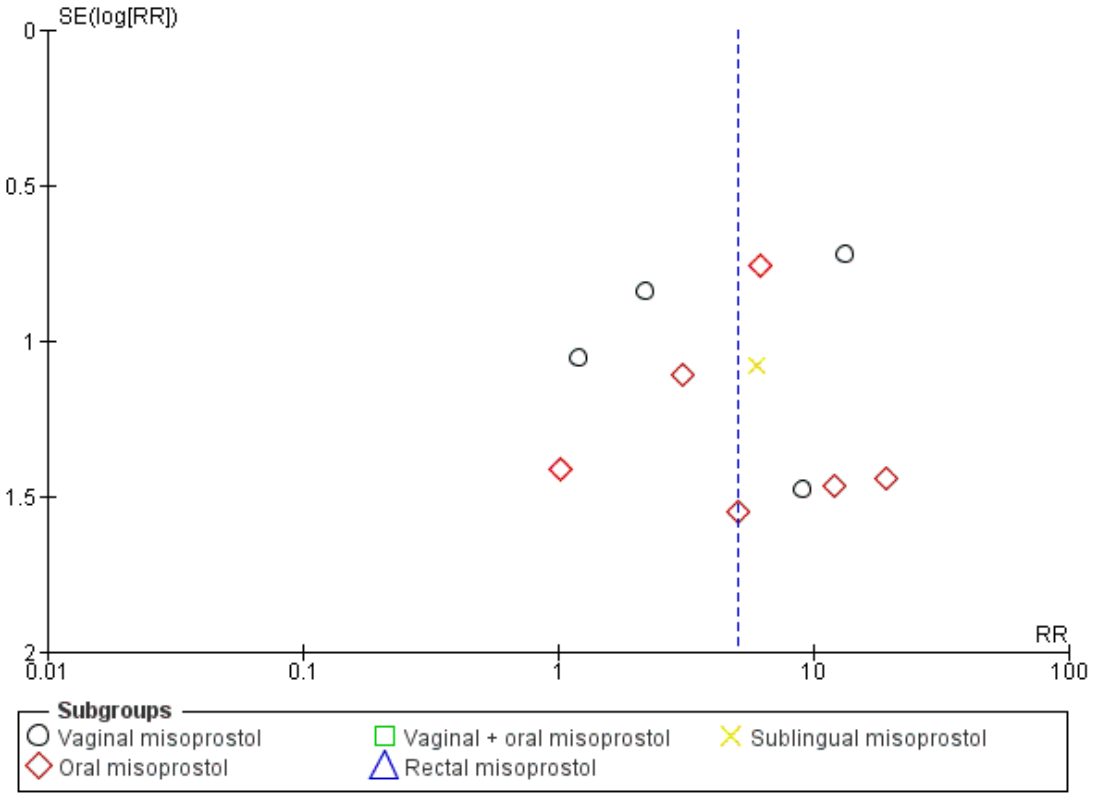
We did not identify any difference between misoprostol and surgery (RR 1.00, 95% CI 0.04 to 22.64; 5 studies, 1248 women), but only one study was estimable, and the review is underpowered to assess this outcome (Analysis 2.3).

Secondary outcomes

Unplanned surgical intervention

We rated the quality of the evidence as low (Summary of findings 2), due to the trials being inevitably unblinded and the potential of publication bias. There was more unplanned surgery with misoprostol (average RR 5.03, 95% CI 2.71 to 9.35; 11 studies, 2690 women, random-effects (Tau^2 = 0.00; P = 0.62; Tau^2, I^2 = 0%)) (Analysis 2.4). The funnel plot displays a potential bias in that there is variation of effect estimates regardless of the study size. This leads to a consideration that there is something affecting the outcome that is not being measured, which is a form of reporting bias (Figure 4).

Figure 4. Funnel plot of comparison: 2 Misoprostol versus surgery, outcome: 2.4 Unplanned surgical intervention.



Blood transfusion

We did not identify any difference for the number of blood transfusions undertaken between misoprostol and surgery (average RR 1.73, 95% CI 0.19 to 16.08; 4 studies, 430 women (Tau^2 = 0.00; Chi^2 P = 0.62; I^2 = 0%)) (Analysis 2.5).

Haemorrhage

There was no information reported on haemorrhage.

Blood loss

There was no information reported on blood loss.

Anaemia

Tau^2

We did not identify any difference in anaemia (average RR 0.83, 95% CI 0.17 to 4.12; 2 studies, 731 women, random-effects (Tau^2 = 0.18; P = 0.28; I^2 = 14%)) (Analysis 2.7).

Days of bleeding

There were more days of bleeding with misoprostol than with surgery (average mean difference (MD) 2.12, 95% CI 1.18 to 3.07; 3 studies, 211 women, random-effects (Tau^2 = 0.19; Chi^2 P = 0.26; I^2 = 25%)) (Analysis 2.8). This difference was also considered clinically significant.

Pain relief

We did not identify a difference with the use of pain relief between women who had misoprostol and women who had surgery (average RR 1.48, 95% CI 0.67 to 3.25; 4 studies, 525 women, random-effects (Tau^2 = 0.50; Chi^2 P < 0.00001; I^2 = 90%)) (Analysis 2.9).

Pelvic infection

We did not identify a difference in the incidence of pelvic infection between women who had misoprostol and those who had surgery (average RR 0.70, 95% CI 0.25 to 1.99; 7 studies, 907 women, random-effects (Tau² = 0.00; Chi² P = 0.60; I² = 0%)) (Analysis 2.10).

Cervical damage

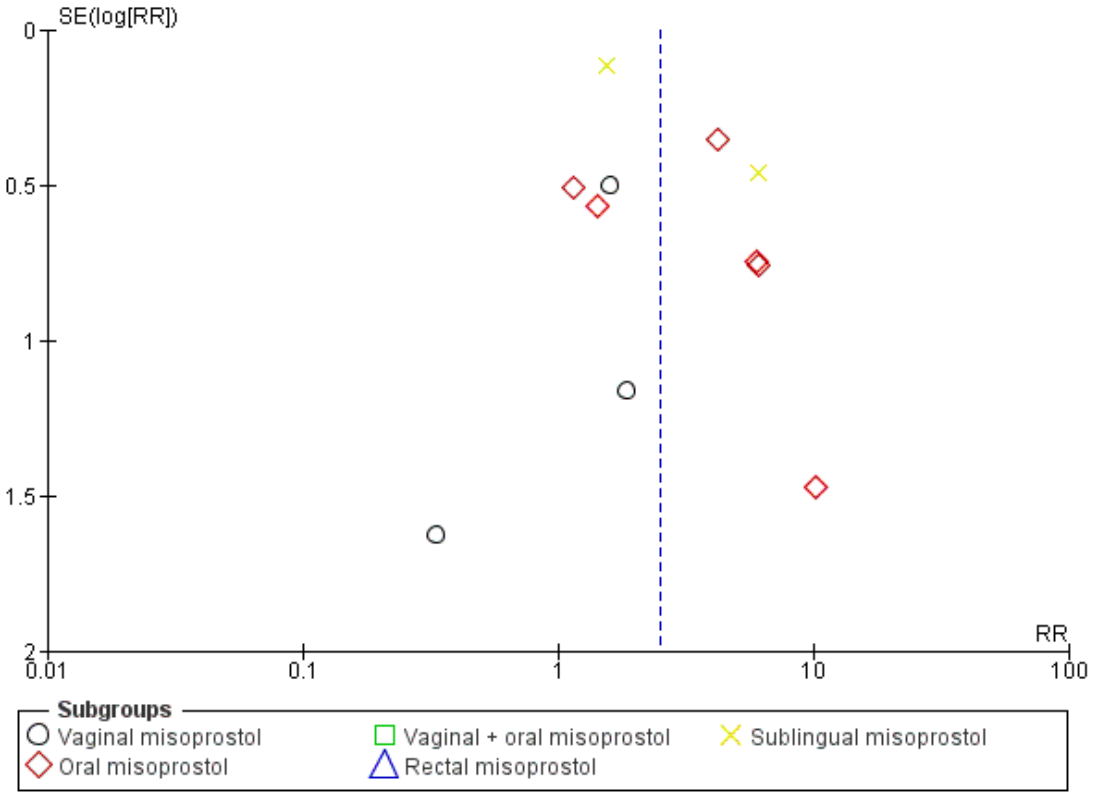
We did not identify a difference in cervical damage, although only one study assessed this outcome (RR 0.07, 95% CI 0.00 to 1.25; 1 study, 189 women) (Analysis 2.11).

Digestive disorders (including nausea, vomiting, diarrhoea)

We rated the quality of the evidence for vomiting and diarrhoea as moderate (Summary of findings 2), due to the trials being inevitably unblinded. We rated the quality of the evidence for nausea specifically, as low due to trials being inevitably unblinded and high heterogeneity.

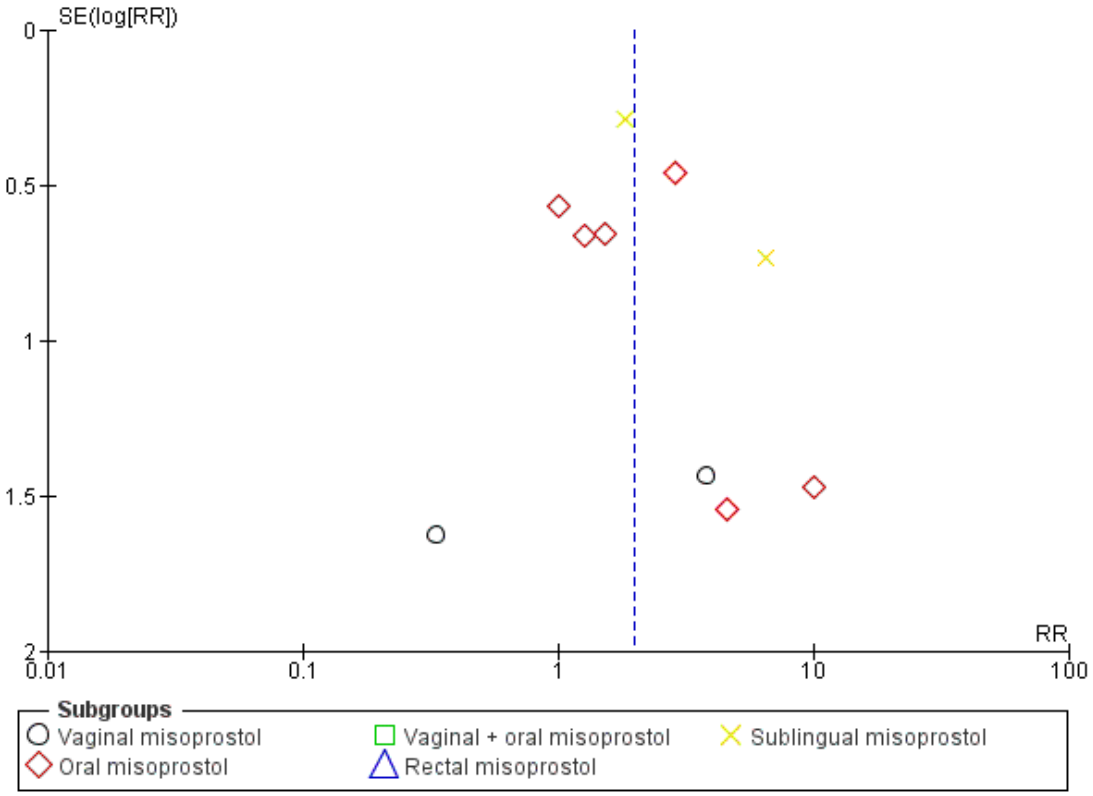
More women had nausea with misoprostol compared with surgery (average RR 2.50, 95% CI 1.53 to 4.09; 11 studies, 3015 women, random-effects (Tau² = 0.31 Chi² P = 0.005; I² = 60%)) (Analysis 2.15, low-quality evidence). This is likely to be clinically significant. The funnel plot does not show existence of a publication bias (Figure 5).

Figure 5. Funnel plot of comparison: 2 Misoprostol versus surgery, outcome: 2.15 Nausea.



More women had vomiting with misoprostol compared with surgery (average RR 1.97, 95% CI 1.36 to 2.85; 10 studies, 2977 women, random-effects (Tau² = 0.00; Chi² P = 0.48; I² = 0%)) (Analysis 2.16, moderate-quality evidence). This may be less clinically significant than the nausea. The funnel plot does not show existence of a publication bias (Figure 6).

Figure 6. Funnel plot of comparison: 2 Misoprostol versus surgery, outcome: 2.16 Vomiting.



More women had diarrhoea with misoprostol compared with surgery (average RR 4.82, 95% CI 1.09 to 21.32; 4 studies, 757 women, random-effects (Tau² = 0.00; Chi² P = 0.98; I² = 0%)) (Analysis 2.17, moderate-quality evidence).

Hypertensive disorders

There was no information reported on hypertensive disorders.

Duration of stay in hospital

There was no information reported on duration of stay in the hospital.

Psychological effects

There was no information reported on psychological effects.

Subsequent fertility

There was no information reported on subsequent fertility.

Women's views/acceptability of method

We rated the quality of the evidence as moderate (Summary of findings 2), due to the trials being inevitably unblinded.

We did not identify a difference in women's satisfaction between misoprostol and surgery when expressed by whether they were satisfied or not (average RR 1.00, 95% CI 0.99 to 1.00; 9 studies, 3349 women, random-effects (Tau² = 0.00; Chi² P = 0.64; I² = 0%)) (Analysis 2.13). Women were very satisfied overall, and satisfaction with misoprostol ranged from 91% to 99% across studies, and satisfaction with surgery ranged from 95% to 100%. When assessed using visual analogue scales, there were more women satisfied with surgery (average standardised mean difference (SMD) 1.01, 95% CI 0.01 to 2.00; 2 studies, 131 women, random-effects (Tau² = 0.41; Chi² P = 0.03; I² = 78%)), but the difference was small and probably not clinically significant (Analysis 2.14). Taken with the findings above, it appears that overall most women are satisfied with the treatment they received.

Pathology of fetal/placental tissue

There was no information reported on pathology of fetal/placental tissue.

Costs

There was no information reported on costs.

3. Vaginal misoprostol versus expectant care (3 studies, 335 women, Analyses 3.1 to 3.7)

For women less than 13 weeks' gestation

Three studies involving 335 women addressed this comparison for women with incomplete miscarriage (Blohm 2005; Shelley 2005; Trinder 2006). There were two further studies that involved both women with incomplete miscarriage and women with intrauterine fetal deaths, but to date we have been unable to obtain the data separated by incomplete miscarriage and intrauterine fetal death for these studies (Bagratee 2004; Ngai 2001).

The studies are of low risk of bias overall. However, blinding of participants and clinicians was only used in one (Blohm 2005), and not the other two studies (Shelley 2005; Trinder 2006).

Diagnosis of incomplete miscarriage and assessment of complete miscarriage after treatment was made using clinical judgement in two studies (Shelley 2005; Trinder 2006), and using ultrasound in the third (Blohm 2005). Assessment of the outcome of complete miscarriage was made at differing times in the three studies: Blohm 2005 assessed at one week, Shelley 2005 at 10 to 14 days, and Trinder 2006 at eight weeks (although there was an assessment at two weeks, findings were not reported separately for women with incomplete miscarriage and women with intrauterine fetal death). We have written to the authors to see if they have earlier data for incomplete miscarriage.

Primary outcomes

Complete miscarriage

Only two of the three studies assessed this outcome (Blohm 2005; Shelley 2005), with the primary outcome for the third study being infection at 14 days (Trinder 2006).

We did not identify a difference in complete miscarriage between vaginal misoprostol and expectant care (average RR 1.23, 95% CI 0.72 to 2.10; 2 studies, 150 women, random-effects (Tau^2 = 0.12; Chi^2 P = 0.02; I^2 = 81%)) (Analysis 3.1). From the clinical perspective, the success rate with vaginal misoprostol ranged from 80% to 81% and for expectant care from 52% to 85%. The heterogeneity may result from the different times at which complete miscarriage was assessed with expectant care. One study assessed at one week and found a success rate of 52% (Blohm 2005), and the other study assessed at 10 to 14 days and found a success rate of 85% (Shelley 2005).

Surgical evacuation

We also did not identify a difference in the need for surgical evacuation between vaginal misoprostol and expectant care (average RR 0.62, 95% CI 0.17 to 2.26; 2 studies, 308 women, random-effects (Tau^2 = 0.78; Chi^2 P = 0.003; I^2 = 89%)) (Analysis 3.2).

Death or serious complication

The outcome of death or serious complication showed no difference (RR 2.91, 95% CI 0.12 to 70.05; 1 study, 126 women), although the review is underpowered to assess this outcome (Analysis 3.3).

Secondary outcomes

Unplanned surgical intervention

We did not identify a difference in unplanned surgical interventions between vaginal misoprostol and expectant care (average RR 0.62, 95% CI 0.17 to 2.26; 2 studies, 308 women, random-effects (Tau^2 = 0.78; Chi^2 P = 0.003; I^2 = 89%)) (Analysis 3.4).

Blood transfusion

We did not identify a difference in the number of blood transfusions undertaken (RR 3.07, 95% CI 0.13 to 74.28; 3 studies, 332 women), although only one study was estimable (Analysis 3.5).

Haemorrhage

There was no information reported on haemorrhage.

Blood loss

There was no information reported on blood loss.

Anaemia

There was no information reported on anaemia.

Days of bleeding

There was no information reported on days of bleeding.

Pain relief

We did not identify a difference in pain relief (average RR 1.12, 95% CI 0.67 to 1.88; 2 studies, 308 women, random-effects (Tau^2 = 0.10; Chi^2 P = 0.08; I^2 = 67%)) (Analysis 3.6).

Pelvic infection

We did not identify a difference in pelvic infection (RR 2.81, 95% CI 0.77 to 10.33; 3 studies, 333 women) (Analysis 3.7).

Cervical damage

There was no information reported on cervical damage.

Digestive disorders (including nausea, vomiting, diarrhoea)

There was no information reported on digestive disorders.

Hypertensive disorders

There was no information reported on hypertensive disorders.

Duration of stay in hospital

There was no information reported on duration of stay in the hospital.

Psychological effects

There was no information reported on psychological effects.

Subsequent fertility

There was no information reported on subsequent fertility.

Women's views/acceptability of method

There was no information reported on women's views.

Pathology of fetal/placental tissue

There was no information reported on pathology of fetal/placental tissue.

Costs

There was no information reported on costs.

4. Vaginal misoprostol versus surgery (6 studies, 549 women, Analyses 4.1 to 4.13)

For women less than 13 weeks' gestation

Six studies involving 549 women addressed this comparison for women with incomplete miscarriage (Ganguly 2010; Moodliar 2005; Patua 2013; Shelley 2005; Trinder 2006;.Zhang 2005). Two further studies involved both women with incomplete miscarriage and women with intrauterine fetal deaths, but to date we have been unable to obtain the data separated by incomplete miscarriage and intrauterine fetal death for these studies, and so we have excluded these studies (Demetroulis 2001; Louey 2000 [pers comm]).
The studies were of low risk of bias overall (Figure 1). However, the nature of the intervention and comparison meant it was not possible to blind participants or clinicians, and it was mostly unclear whether the studies had selective reporting bias, or other biases.
Diagnosis of incomplete miscarriage and assessment of complete miscarriage after treatment was made using clinical judgement in two studies (Shelley 2005; Trinder 2006), and using ultrasound in four studies (Ganguly 2010; Moodliar 2005; Patua 2013; Zhang 2005). Assessment of the outcome of complete miscarriage was made at differing times in the studies: Patua 2013 assessed 24 hours after the last dose of misoprostol or surgical evacuation; Ganguly 2010 assessed at day 3 and day 8 for misoprostol, and day 2 and day 8 for surgical evacuation; Zhang 2005 assessed at three days; Shelley 2005 at 10 to 14 days; Moodliar 2005 at two weeks; and Trinder 2006 at eight weeks (although there was an assessment at two weeks, findings were not reported separately for women with incomplete miscarriage and women with intrauterine fetal death). We have written to the authors to seek these data.

Primary outcomes

Complete miscarriage

Fewer women had complete miscarriage with vaginal misoprostol compared with surgery (RR 0.89, 95% CI 0.84 to 0.95; 5 studies, 364 women) (Analysis 4.1). However, from the clinical perspective the success rate was high in both groups, vaginal misoprostol ranged from 80% to 91% and for surgery from 89% to 100%.

Surgical evacuation

Fewer women had surgical evacuation with vaginal misoprostol compared with women who were given surgery straight away (average RR 0.16, 95% CI 0.07 to 0.35; 4 studies, 411 women, random-effects (Tau^2 = 0.52; Chi^2 P = 0.002; I^2 = 80%)) (Analysis 4.2). This finding was perhaps not surprising as the comparison group was surgical intervention, but it is an important outcome to assess as clinical management would be to use surgery if misoprostol failed. This reduction in the use of surgery with vaginal misoprostol helps to confirm the success of this intervention. The reasons for the heterogeneity were unclear.

Death or serious complication

We did not identify a difference in the composite outcome of death or serious complications (RR 1.00, 95% CI 0.04 to 22.64; 2 studies, 132 women, (although only one was estimable); however, the review is underpowered to assess this outcome (Analysis 4.3).

Secondary outcomes

Unplanned surgical intervention

In the vaginal misoprostol group, there was a higher incidence of unplanned surgical intervention (average RR 4.29, 95% CI 1.24 to 14.87; 4 studies, 411 women (Tau^2 = 0.67; Chi^2 P = 0.16; I^2 = 42%)) (Analysis 4.4). Again, this finding is unsurprising, as surgery is the comparative intervention and one would anticipate that few additional operations would be required if surgery was successful.

Blood transfusion

We did not identify a difference in the number of blood transfusions undertaken (RR 1.82, 95% CI 0.21 to 15.70; 3 studies, 241 women) (Analysis 4.5).

Haemorrhage

There was no information reported on haemorrhage.

Blood loss

There was no information reported on blood loss.

Anaemia

We did not identify a difference in anaemia (RR 1.71, 95% CI 0.24 to 12.24; 1 study, 36 women) (Analysis 4.6).

Days of bleeding

Women treated with vaginal misoprostol had more days of bleeding than women treated with surgery (MD 2.76, 95% CI 1.55 to 3.97; 2 studies, 131 women) (Analysis 4.7).

Pain relief

Women treated with vaginal misoprostol used more pain relief than women treated with surgery (RR 1.75, 95% CI 1.21 to 2.54; 3 studies, 313 women) (Analysis 4.8).

Pelvic infection

We did not identify a difference in pelvic infection (RR 1.27, 95% CI 0.37 to 4.42; 4 studies, 338 women) (Analysis 4.9).

Cervical damage

There was no information reported on cervical damage.

Digestive disorders (including nausea, vomiting, diarrhoea)

We did not identify a difference in the number of women with nausea (RR 1.37, 95% CI 0.58 to 3.22; 3 studies, 156 women) (Analysis 7.24), vomiting (RR 1.48, 95% CI 0.25 to 8.93; 2 studies, 131 women) (Analysis 7.25), or diarrhoea (RR 4.30, 95% CI 0.52 to 35.36; 2 studies, 131 women) (Analysis 7.26).

Hypertensive disorders

There was no information reported on hypertensive disorders.

Duration of stay in hospital

There was no information reported on duration of stay in the hospital.

Psychological effects

There was no information reported on psychological effects.

Subsequent fertility

There was no information reported on subsequent fertility.

Women's views/acceptability of method

Women were more satisfied with surgery (average SMD 1.01, 95% CI 0.01 to 2.00; 2 studies, 131 women, random-effects (Tau^2 = 0.41; Chi^2 P = 0.03; I^2 = 78%)), but the difference was small and based on just two small studies (Analysis 4.10). Reasons for the heterogeneity were unclear.

Pathology of fetal/placental tissue

There was no information reported on pathology of fetal/placental tissue.

Costs

There was no information reported on costs.

5. Oral misoprostol versus surgery (7 studies, 1884 women, Analyses 5.1 to 5.11)

For women less than 13 weeks' gestation

Seven studies involving 1884 women addressed this comparison for women with incomplete miscarriage (Bique 2007; Chigbu 2012; Dao 2007; Montesinos 2011; Shwekerela 2007; Taylor 2011; Weeks 2005). We identified a further study involving both women with incomplete miscarriage and women with intrauterine fetal deaths, but the authors, although they were able to supply additional data, were unable to separate outcomes by women with incomplete miscarriage and women with intrauterine death and so we excluded this study (Chung 1999).

The included studies were of low risk of bias overall (Figure 1), with all having adequate sequence generation and concealment allocation. Blinding was not possible when comparing medical treatment with surgery. Four of the studies had little loss to follow-up and exclusions after randomisation (Bique 2007; Chigbu 2012; Dao 2007; Shwekerela 2007). However, one study, although it had no loss to follow-up at six days, had considerable loss to follow-up at one to two weeks (33% in the misoprostol group and 45% in the group having surgery) which was not similar between the groups (Weeks 2005). This seemed to arise from women returning home to their communities and not coming back for follow-up appointments, and this was fully discussed by the authors (Weeks 2005). Sensitivity analysis was not undertaken because outcomes at six days did not appear to be subject to bias.

Diagnosis of incomplete miscarriage and assessment of complete miscarriage after treatment was made using clinical judgement in four studies (Bique 2007; Chigbu 2012; Shwekerela 2007; Weeks 2005), and using ultrasound, if necessary, in three studies (Dao 2007; Montesinos 2011; Taylor 2011). Assessment of the outcome of complete miscarriage was made at seven days in all seven studies (Bique 2007; Chigbu 2012; Dao 2007; Montesinos 2011; Shwekerela 2007; Taylor 2011; Weeks 2005).

Primary outcomes

Complete miscarriage

There was no difference identified in the number of complete miscarriages with oral misoprostol compared with surgery (average RR 0.98, 95% CI 0.95 to 1.00; 7 studies, 1884 women, random-effects (Tau^2 = 0.00; Chi^2 = 0.004; I^2 = 69%)) (Analysis 5.1). In addition, in terms of clinical impact, the success rate was high in both groups, for oral misoprostol it ranged from 91% to 99% and surgery ranged from 91% to 100%.

Surgical evacuation

Fewer women had surgical evacuation with oral misoprostol (average RR 0.04, 95% CI 0.02 to 0.07; 7 studies, 1884 women, random-effects (Tau^2 = 0.38. Chi^2 P = 0.006; I^2 = 67%)) (Analysis 5.2). The reasons for the heterogeneity were unclear.

Death or serious complication

There were no data for this outcome.

Secondary outcomes

Unplanned surgical intervention

There were more women needing unplanned surgical intervention in the oral misoprostol group (RR 6.27, 95% CI 2.57 to 15.31; 6 studies, 1584 women) (Analysis 5.3).

Blood transfusion

It was not possible to produce a RR with the data (Analysis 5.4).

Haemorrhage

There was no information reported on haemorrhage.

Blood loss

There was no information reported on blood loss.

Anaemia

There was no information reported on anaemia.

Days of bleeding

There was no information reported on days of bleeding.

Pain relief

There was less pain relief required with oral misoprostol than with surgery (RR 0.85, 95% CI 0.77 to 0.92; 1 study, 212 women), but the difference was small and most women used pain relief whether they had misoprostol or surgery (Analysis 5.5).

Pelvic infection

We did not identify a difference in pelvic infection (RR 0.26, 95% CI 0.03 to 2.41; 2 studies, 489 women) (Analysis 5.6).

Cervical damage

We did not identify a difference in cervical damage (RR 0.07, 95% CI 0.00 to 1.25; 1 study, 189 women) (Analysis 5.7).

Digestive disorders

More women experienced nausea (RR 3.24, 95% CI 2.10 to 4.98; 6 studies, 1700 women) (Analysis 5.9), and vomiting (RR 1.99, 95% CI 1.18 to 3.34; 6 studies, 1687 women) with oral misoprostol compared with surgery (Analysis 5.10), but we did not identify a difference in the incidence of diarrhoea (RR 5.79, 95% CI 0.70 to 47.64; 2 studies, 626 women) (Analysis 5.11).

Hypertensive disorders

There was no information reported on hypertensive disorders.

Duration of stay in hospital

There was no information reported on duration of stay in the hospital.

Psychological effects

There was no information reported on psychological effects.

Subsequent fertility

There was no information reported on subsequent fertility.

Women's views/acceptability of method

We did not identify a difference in women's satisfaction (RR 0.99, 95% CI 0.98 to 1.01; 7 studies, 1875 women) (Analysis 5.8).

Pathology of fetal/placental tissue

There was no information reported on pathology of fetal/placental tissue.

Costs

There was no information reported on costs.

6. Vaginal plus oral misoprostol versus surgery (1 study, 80 women, Analyses 6.1 to 6.4)

For women less than 13 weeks' gestation

One study involving 80 women assessed this comparison (Sahin 2001).

The study was at high risk of bias with uncertainty around sequence generation, allocation concealment, selective reporting bias, and other potential biases, and it was not possible to blind participants and clinicians.

Assessment of incomplete miscarriage was undertaken using ultrasound and assessment of outcomes was undertaken at 10 days.

Primary outcomes

Complete miscarriage

There was no difference identified in incomplete miscarriage (RR 0.95, 95% CI 0.87 to 1.04; 1 study, 80 women) (Analysis 6.1). In clinical terms, the success in this one study was 95% with medical treatment and 100% with surgery.

Surgical evacuation

There was less need for surgical evacuation with misoprostol than with surgery (RR 0.04, 95% CI 0.01 to 0.18; 1 study, 80 women) (Analysis 6.2).

Death or serious complication

Not reported.

Secondary outcomes

Unplanned surgical intervention

There was no information reported on unplanned surgical intervention.

Blood transfusion

There was no information reported on blood transfusion.

Haemorrhage

There was no information reported on haemorrhage.

Blood loss

There was no information reported on blood loss.

Anaemia

There was no information reported on anaemia.

Days of bleeding

There were fewer days of bleeding with surgery compared with vaginal plus oral misoprostol (MD 1.55, 95% CI 0.58 to 2.52; 1 study, 80 women) (Analysis 6.3).

Pain relief

There was no information reported on pain relief.

Pelvic infection

We did not identify a difference in pelvic infection (RR 0.50, 95% CI 0.05 to 5.30; 1 study, 80 women) (Analysis 6.4).

Cervical damage

There was no information reported on cervical damage.

Digestive disorders (including nausea, vomiting, diarrhoea)

There was no information reported on digestive disorders.

Hypertensive disorders

There was no information reported on hypertensive disorders.

Duration of stay in hospital

There was no information reported on duration of stay in the hospital.

Psychological effects

There was no information reported on psychological effects.

Subsequent fertility

There was no information reported on subsequent fertility.

Women's views/acceptability of method

There was no information reported on women's views.

Pathology of fetal/placental tissue

There was no information reported on pathology of fetal/placental tissue.

Costs

There was no information reported on costs.

7. Sublingual misoprostol versus surgery (2 studies, 1534 women, Analyses 7.1 to 7.8)

For women less than 13 weeks' gestation

Two studies involving 1534 women addressed this comparison for women with incomplete miscarriage (Dabash 2010; Shochet 2012).

Dabash 2010 was of low risk of bias overall (Figure 1), having adequate sequence generation and concealment allocation. Blinding was not possible when comparing medical treatment with surgery. However, for the second study (Shochet 2012), it was unclear how sequence generation and allocation concealment were conducted. Diagnosis of incomplete miscarriage and assessment of complete miscarriage after treatment was made using clinical judgement and use of ultrasound, as needed, in both studies. Assessment of the outcome of complete miscarriage was made at one week follow-up in both studies.

Primary outcomes

Complete miscarriage

There was no difference identified in the number of complete miscarriages (RR 0.96, 95% CI 0.95 to 0.98; 2 studies, 1534 women) (Analysis 7.1), with the success rate being 94% to 98% with sublingual misoprostol and 99% to 100% with surgery.

Surgical evacuation

There was less need for surgical evacuation with misoprostol than with surgery (RR 0.02, 95% CI 0.01 to 0.04; 1 study, 695 women) (Analysis 7.2).

Death or serious complications

Not reported.

Secondary outcomes

Unplanned surgical intervention

In the sublingual misoprostol group, there was a higher incidence of unplanned surgical intervention (average RR 5.98, 95% CI 0.72 to 49.43; 1 study, 695 women) (Analysis 7.3). Again, this finding is unsurprising, as surgery is the comparative intervention and one would anticipate that few additional operations would be required if surgery was successful.

Blood transfusion

There was no information reported on blood transfusion.

Haemorrhage

There was no information reported on haemorrhage.

Blood loss

There was no information reported on blood loss.

Anaemia

We did not identify a difference in anaemia (RR 0.33, 95% CI 0.03 to 3.18; 1 study, 695 women) (Analysis 7.4).

Days of bleeding

There was no information reported on days of bleeding.

Pain relief

There was no information reported on pain relief.

Pelvic infection

There was no information reported on pelvic infection

Cerivcal damage

There was no information reported on cervical damage.

Digestive disorders

Women in the misoprostol group were more likely to experience gastrointestinal issues compared to the women in the surgery group (RR 3.90, 95%CI 1.81 to 8.42; 1 study, 516 women) (Analysis 7.5). More women experienced nausea in the misoprostol group (RR 1.86, 95% CI 1.48 to 2.32; 2 studies, 1159 women) (Analysis 7.7), and vomiting (RR 2.42, 95% CI 1.43 to 4.10; 2 studies, 1159 women) (Analysis 7.8).

Hypertensive disorders

There was no information reported on hypertensive disorders.

Duration of stay in hospital

There was no information reported on duration of stay in the hospital.

Psychological effects

There was no information reported on psychological effects.

Subsequent fertility

There was no information reported on subsequent fertility.

Women's views/acceptability of method

We did not identify a difference in women's satisfaction towards their method (RR 0.99, 95% CI 0.98 to 1.01; 2 studies, 1474 women) (Analysis 7.6).

Pathology of fetal/placental tissue

There was no information reported on pathology of fetal/placental tissue.

Costs

There was no information reported on costs.

8. Vaginal misoprostol versus oral misoprostol (1 study, 201 women, Analyses 8.1 to 8.7)

For women less than 13 weeks' gestation

One study involving 201 women addressed this comparison for women with incomplete miscarriage (Pang 2001). One further study involved both women with incomplete miscarriage and women with intrauterine fetal deaths, but to date we have been unable to obtain the data separated by incomplete miscarriage and

intrauterine fetal death for this study, and so we have excluded it from this review (Machtinger 2004).
The risk of bias in Pang 2001 was at low risk in terms of having adequate sequence generation and concealment allocation, and appeared to be free of other potential sources of bias, however, it was not clear whether participants, clinicians and assessors were blinded to the intervention given (Figure 1).
Assessment of incomplete miscarriage was undertaken using ultrasound and assessment of outcomes was undertaken at one day after treatment.

Primary outcomes

Complete miscarriage

We did not identify a difference in the number of complete miscarriages (RR 0.94, 95% CI 0.76 to 1.16; 1 study, 198 women) (Analysis 8.1), with the success rate being 61% with vaginal misoprostol and 65% with oral misoprostol, both assessed on day one.

Surgical evacuation

We did not identify a difference in surgical evacuation (RR 1.11, 95% CI 0.77 to 1.60; 1 study, 198 women) (Analysis 8.2).

Death or serious complications

Not reported.

Secondary outcomes

Unplanned surgical intervention

We did not identify a difference in unplanned surgical intervention (RR 0.36, 95% CI 0.01 to 8.80; 1 study, 186 women) (Analysis 8.3).

Blood transfusion

There was no information reported on blood transfusion.

Haemorrhage

There was no information reported on haemorrhage.

Blood loss

There was no information reported on blood loss.

Anaemia
There was no information reported on anaemia.
Days of bleeding
There as no information reported on days of bleeding.

Pain relief

We did not identify a difference in pain relief (RR 1.43, 95% CI 0.93 to 2.17; 1 study, 186 women) (Analysis 8.4).

Pelvic infection

There was no information reported on pelvic infection

Cerivcal damage

There was no information reported on cervical damage.

Digestive disorders

We did not identify any differences in the number of women experiencing nausea (RR 0.63, 95% CI 0.26 to 1.54; 1 study involving 198 women) (Analysis 8.5), and vomiting (RR 0.36, 95% CI 0.07 to 1.75; 1 study, 198 women) (Analysis 8.6).
There was a reduction in the incidence of diarrhoea for women using vaginal misoprostol compared with oral misoprostol (RR 0.21, 95% CI 0.12 to 0.36; 1 study, 198 women) (Analysis 8.7).

Hypertensive disorders

There was no information reported on hypertensive disorders.

Duration of stay in hospital

There was no information reported on duration of stay in the hospital.

Psychological effects

There was no information reported on psychological effects.

Subsequent fertility

There was no information reported on subsequent fertility.

Women's views/acceptability of method

There was no information reported on women's views.

Pathology of fetal/placental tissue

There was no information reported on pathology of fetal/placental tissue.

Costs

There was no information reported on costs.

9. Oral misoprostol 600 ug versus oral misoprostol 1200 ug (2 studies, 469 women, Analyses 9.1 to 9.8)

For women less than 13 weeks' gestation

Two studies involving 469 women addressed this comparison for women with incomplete miscarriage (Blanchard 2004; Ngoc 2005).

Blanchard 2004 was on the whole at low risk of bias, with adequate sequence generation, concealment of allocation, low loss to follow-up, and other sources of bias were not apparent. However, there was no blinding of participants, clinicians and assessors, and it was unclear whether there was selective reporting bias. Ngoc 2005 was similar, but it was unclear whether there was adequate allocation concealment (Figure 1).

Primary outcomes

Complete miscarriage

We did not identify a difference in complete miscarriage (RR 1.00, 95% CI 0.93 to 1.07; 2 studies, 464 women) (Analysis 9.1).

Surgical evacuation

We did not identify a difference in surgical evacuation (RR 0.76, 95% CI 0.29 to 1.99; 1 study, 295 women) (Analysis 9.2). The success rate with the single 600 ug dose ranged from 66% to 95%, and the success rate with the repeat 600 ug dose (total 1200 ug) ranged from 67% to 94%.

Death or serious complication

One study provided data (Ngoc 2005), but it was not possible to produce a RR (Analysis 9.3).

Secondary outcomes

Unplanned surgical intervention

We did not identify a difference in the number of unplanned surgical interventions (RR 0.76, 95% CI 0.29 to 1.99; 1 study, 295 women) (Analysis 9.4).

Blood transfusion

There was no information reported on blood transfusion.

Haemorrhage

There was no information reported on haemorrhage.

Blood loss

There was no information reported on blood loss.

Anaemia

There was no information reported on anaemia.

Days of bleeding

There was no information reported on days of bleeding.

Pain relief

There was no information reported on pain relief.

Pelvic infection

There was no information reported on pelvic infection.

Cervical damage

There was no information reported on cervical damage.

Digestive disorders

We did not identify a difference between the two doses of oral misoprostol for nausea (average RR 1.19, 95% CI 0.57 to 2.46; 2 studies, 463 women, random-effects (Tau^2 = 0.19; Chi^2 P = 0.07; I^2 = 70%)) (Analysis 9.6), or vomiting (RR 1.01, 95% CI 0.60 to 1.72; 2 studies, 463 women) (Analysis 9.7).

There was a reduction in the incidence of diarrhoea for women allocated to one dose of misoprostol (RR 0.73, 95% CI 0.55 to 0.97; 1 study, 294 women) (Analysis 9.8). The CI and the data being from one small study, makes the clinical significance unclear.

Hypertensive disorders

There was no information reported on hypertensive disorders.

Duration of stay in hospital

There was no information reported on duration of stay in the hospital.

Psychological effects

There was no information reported on psychological effects.

Subsequent fertility

There was no information reported on subsequent fertility.

Women's views/acceptability of method

We did not identify a difference in women's satisfaction (RR 1.02, 95% CI 0.96 to 1.09; 2 studies, 460 women) (Analysis 14.5).

Pathology of fetal/placental tissue

There was no information reported on pathology of fetal/placental tissue.

Costs

There was no information reported on costs.

10. Oral mifepristone + vaginal misoprostol versus surgery (1 study, 19 women, Analyses 10.1 to 10.2)

Niinimaki 2006 included women with many kinds of miscarriage (missed abortion, anembryonic pregnancies, incomplete miscarriage) but the authors were able to send us the data split by the types of miscarriage. The study also involved women at less than 24 weeks' gestation, some of whom were less than 13 weeks and some not.

For women less than 13 weeks' gestation

For the 16 women who were less than 13 weeks' gestation, treatments were equally successful with 10/10 (100%) women in the medical group and 6/6 (100%) women in the surgical group achieving complete miscarriage. There were no additional surgical evacuations required and none of the women had pelvic infections.

For women 13 to 23 weeks' gestation

For the three women who were between 13 and 24 weeks' gestation, treatments again were equally successful with 1/1 (100%) women in the medical group and 2/2 (100%) women in the surgical group achieving complete miscarriage. There were no additional surgical evacuations required and none of the women had pelvic infections.

11. Vaginal prostaglandin E1 (gemeprost) versus surgery (1 study, 34 women, Analyses 11.1)

For women less than 13 weeks' gestation

One study involving 34 women compared vaginal prostaglandin E1 (gemeprost) with surgery (Clevin 2001). The study was of uncertain risk of bias. It had adequate sequence generation and low risk of other potential sources of bias. However, the allocation concealment was unclear, as was the completeness of the outcome data and potential for selective reporting bias. It was not possible to blind participants and clinicians.

Primary outcomes

None of the prespecified primary outcomes were reported.

Secondary outcomes

Unplanned surgical intervention

Although data were reported on this outcome it was not possible to report a RR (Analysis 11.1).

Blood transfusion

There was no information reported on blood transfusion.

Haemorrhage

There was no information reported on haemorrhage.

Blood loss

There was no information reported on blood loss.

Anaemia

There was no information reported on anaemia.

Days of bleeding

There was no information reported on days of bleeding.

Pain relief

There was no information reported on pain relief.

Pelvic infection

There was no information reported on pelvic infection.

Cervical damage

There was no information reported on cervical damage.

Digestive disorders

There was no information reported on digestive disorders.

Hypertensive disorders

There was no information reported on hypertensive disorders.

Duration of stay in hospital

There was no information reported on duration of stay in the hospital.

Psychological effects

There was no information reported on psychological effects.

Subsequent fertility

There was no information reported on subsequent fertility.

Women's views/acceptability of method

There was no information reported on women's views/acceptability of method.

Pathology of fetal/placental tissue

There was no information reported on pathology of fetal/placental tissue.

Costs

There was no information reported on costs.

12. Sublingual misoprostol versus oral misoprostol (2 studies, 358 women, Analyses 12.1 to 12.7)

For women less than 13 weeks' gestation

Two studies involving 358 women looked at this comparison (Diop 2009; Paritakul 2010). The studies were at low risk of bias with adequate sequence generation and allocation concealment. However, the studies were not blinded (Figure 1).

Primary outcomes

Complete miscarriage

We found no difference between sublingual and oral misoprostol in terms of complete miscarriage (RR 0.99, 95% CI 0.94 to 1.05; 2 studies, 358 women) (Analysis 12.1).

Surgical evacuation

There was also no difference in surgical evacuation between the two routes of administration of misoprostol (RR 1.01, 95% CI 0.39 to 2.63; 1 study, 294 women) (Analysis 12.2).

Death or serious morbidity

There were no deaths or serious morbidity amongst the women in these trials.

Secondary outcomes

Unplanned surgical intervention

There was no information reported on unplanned surgical intervention.

Blood transfusion

There was no information reported on blood transfusion.

Haemorrhage

There was no information reported on haemorrhage.

Blood loss

There was no information reported on blood loss.

Anaemia

There was no information reported on anaemia.

Days of bleeding

There was no information reported on days of bleeding.

Pain relief

There was no information reported on pain relief.

Pelvic infection

There was no information reported on pelvic infection.

Cervical damage

There was no information reported on cervical damage.

Digestive disorders

There was no difference in nausea between the two routes of administration of misoprostol (RR 0.78, 95% CI 0.49 to 1.23; 2 studies, 358 women) (Analysis 12.4)

There was also no difference in vomiting between the two routes of administration of misoprostol (RR 1.01, 95% CI 0.14 to 7.10; 2 studies, 358 women) (Analysis 12.5)

There was also no difference in diaorrhea between the two routes of administration of misoprostol (RR 1.58, 95% CI 0.66 to 3.76; 2 studies, 358 women) (Analysis 12.6)

Hypertensive disorders

There was no information reported on hypertensive disorders.

Duration of stay in hospital

There was no information reported on duration of stay in the hospital.

Psychological effects

There was no information reported on psychological effects.

Subsequent fertility

There was no information reported on subsequent fertility.

Women's views/acceptability of method

We did not identify a difference between the two routes of administration of misoprostol for this outcome. (RR 0.99, 95% CI 0.95 to 1.03; 2 studies, 358 women) (Analysis 12.7)

Pathology of fetal/placental tissue

There was no information reported on pathology of fetal/placental tissue.

Costs

There was no information reported on costs.

Oral misoprostol versus expectant care (no studies)

There were no studies that addressed this comparison.

Rectal misoprostol versus expectant care (no studies)

There were no studies that addressed this comparison.

Sublingual misoprostol versus expectant care (no studies)

There were no studies that addressed this comparison.

Rectal misoprostol versus surgery (no studies)

There were no studies that addressed this comparison.

Rectal misoprostol versus oral misoprostol (no studies)

There were no studies that addressed this comparison.

ADDITIONAL SUMMARY OF FINDINGS [*Explanation*]

Misoprostol compared to surgery for incomplete miscarriage

Patient or population: incomplete miscarriage
Setting: clinics and hospitals in Australia, Burkina Faso, Egypt, Ecuador, Ghana, India, Mauritania, Mozambique, Niger, Nigeria, South Africa, Tanzania, Turkey, Uganda, USA
Intervention: misoprostol
Comparison: surgery

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with surgery	Risk with Misoprostol				
Complete miscarriage	Study population		RR 0.96 (0.94 to 0.98)	3862 (15 RCTs)	⊕◯◯◯ VERY LOW [1,2,3]	
	992 per 1000	963 per 1000 (943 to 982)				
	Moderate					
	1000 per 1000	970 per 1000 (950 to 990)				
Surgical evacuation	Study population		RR 0.05 (0.02 to 0.11)	3070 (13 RCTs)	⊕◯◯◯ VERY LOW [1,2,4,5]	
	985 per 1000	49 per 1000 (20 to 108)				
	Moderate					
	1000 per 1000	50 per 1000 (20 to 110)				
Unplanned surgical intervention	Study population		RR 5.03 (2.71 to 9.35)	2690 (11 RCTs)	⊕⊕◯◯ LOW [1,6]	

	8 per 1000	38 per 1000 (21 to 71)			
	Moderate				
	9 per 1000	45 per 1000 (24 to 83)			
Women's views/ acceptability of method	Study population		RR 1.00 (0.99 to 1.00)	3349 (9 RCTs)	⊕⊕⊕◯ MODERATE [7]
	981 per 1000	981 per 1000 (971 to 981)			
	Moderate				
	982 per 1000	982 per 1000 (972 to 982)			
Nausea	Study population		RR 2.50 (1.53 to 4.09)	3015 (11 RCTs)	⊕⊕◯◯ LOW [1,2]
	84 per 1000	210 per 1000 (128 to 343)			
	Moderate				
	44 per 1000	110 per 1000 (67 to 179)			
Vomiting	Study population		RR 1.97 (1.36 to 2.85)	2977 (10 RCTs)	⊕⊕⊕◯ MODERATE [1]
	29 per 1000	56 per 1000 (39 to 82)			
	Moderate				
	20 per 1000	39 per 1000 (27 to 56)			

Diarrhoea	Study population		RR 4.82 (1.09 to 21.32)	757 (4 RCTs)	⊕⊕⊕◯ MODERATE [1]
	0 per 1000	0 per 1000 (0 to 0)			

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).
CI: confidence interval; **RCT**: randomised controlled trial; **RR:** risk ratio.

GRADE Working Group grades of evidence
High-quality: We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate-quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low-quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Very low-quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1] Lack of blinding.
[2] High heterogeneity.
[3] Lack of smaller studies showing a RR more than 1.
[4] Wide confidence interval crossing the line of no effect and small sample size.
[5] Asymmetrical funnel plot.
[6] Variation of effect size regardless of the study size.
[7] Downgraded for overall risk of bias (limitations in design).

DISCUSSION

Virtually all the studies we identified involved women less than 13 weeks' pregnant; there was one study that included three women greater than 13 weeks' pregnant (Niinimaki 2006). Misoprostol was the drug studied most frequently and it was assessed against expectant care and surgery, and the possible routes of administration were vaginal, oral, vaginal plus oral, sublingual, and rectal.

Summary of main results

The limited data available for all these comparisons can be summarised as follows.

Misoprostol compared with expectant care (Comparison 1): we did not identify any differences between misoprostol and expectant care, although the review was underpowered to assess this comparison with only three studies involving 335 women. Vaginal misoprostol was the only route of administration used in these comparisons and further studies would be needed to be sure of the findings.

Misoprostol compared with surgery (Comparison 2): misoprostol appeared slightly less effective than surgery, but the difference was probably not clinically relevant, with the success rate for both treatments being high. There was a large reduction in surgery required when misoprostol was used. There was more blood loss with misoprostol, although cervical damage seemed less; however, this was assessed in only one study with possible risk of bias in losses to follow-up. There was more nausea and vomiting with misoprostol (particularly oral misoprostol), but we did not identify a difference in women's satisfaction.

Vaginal misoprostol compared with expectant care (Comparison 3): we did not identify any differences between vaginal misoprostol compared with expectant care in terms of women achieving a complete miscarriage. However, in one study vaginal misoprostol was more effective than expectant care (Blohm 2005), and in the other study was equally effective (Shelley 2005). This difference seems to lie in the differing success in the expectant care group between the two studies. Complete miscarriage was 52% (32/64) in the study assessing this at one week (Blohm 2005), and 85% (12/14) in the study assessing it at two weeks (Shelley 2005). This is in contrast to the success rates with vaginal misoprostol which were 81% (52/64) and 80% (8/10), respectively. It may be, therefore, that if women are prepared to wait longer, then more might achieve spontaneous miscarriage without the use of vaginal misoprostol. However, the numbers of participants in both these studies was small. We did not identify any differences in the other outcomes assessed (surgical evacuation, death or serious complications, blood transfusions, pain relief, pelvic infection). There was no information about women's views of these two forms of care.

Vaginal misoprostol compared with surgery (Comparison 4): there was a small reduction in women achieving a complete miscarriage with vaginal misoprostol compared with surgery. However, vaginal misoprostol still showed a success rate of between 80% to 91%. There was a large reduction in the use of surgery and no difference in death or serious complications. The mean number of days of bleeding was higher with misoprostol and there was more need for pain relief. There was no difference in the other outcomes assessed (blood transfusion, anaemia, pelvic infection, nausea, vomiting, diarrhoea).

Oral misoprostol compared with surgery (Comparison 5): we did not identify a difference between oral misoprostol compared with surgery in terms of women achieving a complete miscarriage. There was a large reduction in the use of surgery, and deaths or serious complications were not reported. There was less pain relief needed with oral misoprostol, but increased nausea and vomiting. There were no difference in other outcomes assessed (pelvic infection, cervical damage, diarrhoea).

Vaginal plus oral misoprostol compared with surgery (Comparison 6): based on one study of 80 women, we did not identify any differences for complete miscarriage (success rates from 95% to 100%), days of bleeding and pelvic infection. There was a reduction in the use of surgery with medical management.

Sublingual misoprostol compared with surgery (Comparison 7): we did not identify a difference between sublingual misoprostol compared with surgery in terms of women achieving a complete miscarriage. There was a reduction in the use of surgery with medical management. There was increased nausea and vomiting with sublingual misoprostol.

Vaginal misoprostol compared with oral misoprostol (Comparison 8): we did not identify a difference between vaginal misoprostol compared with oral misoprostol in terms of women achieving a complete miscarriage or in the need for additional surgical intervention. The incidence of diarrhoea was less with vaginal misoprostol compared with the oral route, but there was no difference in other outcomes assessed (pain relief, nausea, vomiting).

600 ug oral misoprostol compared with 1200 ug oral misoprostol (Comparison 9): the only difference identified in this comparison was that more women experienced diarrhoea with the higher dose.

Sublingual misoprostol compared with oral misoprostol (Comparison 12): we did not identify a difference between the two groups.

Other comparisons: for other comparisons there were either no studies or the studies provided insufficient data.

Women's views: the only study that assessed women's views in any detail was a publication by Harwood 2008, as part of the study on vaginal misoprostol versus surgery (Zhang 2005). The 652 women in this multicentre randomised controlled trial were asked prospectively to complete a daily diary of any symptoms experienced for the two weeks after treatment. The women also completed questionnaires assessing quality of life, depression, stress, and treatment acceptability at two weeks after treatment. Although a few differences were observed in some of the individual measures, overall there was no difference in the mean scores for quality of life, although vaginal misoprostol was associated with higher levels of pain than surgery. Overall treatment acceptability was similar,

and these findings can help to inform the focus of counselling for women choosing a treatment option.

Overall completeness and applicability of evidence

The review is probably underpowered to assess the effectiveness of medical treatments for incomplete miscarriage. In addition, nearly all studies were focused on women less than 13 weeks gestation and there is a need for more evidence on women more than 13 weeks gestation.

In terms of study settings, the evidence stems from both low-income to high-income countries. The majority of the studies took place in Africa and Southeast Asia while the remaining seven studies were in Europe and USA.

One study published by Smith 2009 but part of the MIST trial, undertook long-term follow-up to assess any potential impact on subsequent fertility (Trinder 2006). They concluded that the method of miscarriage management did not affect subsequent pregnancy rates with around four in five women giving birth within five years of the index miscarriage. Women can be reassured that long-term fertility concerns need not affect their choice of miscarriage management.

Quality of the evidence

The risk of bias of studies was generally low, although it is hard to assess if there has been selective reporting bias.

We assessed the quality of evidence using GRADE for the two main comparisons (Atkins 2004): misoprostol versus expectant management and misoprostol versus surgery. The majority of the evidence was of low-quality or very low-quality. For the misoprostol versus expectant management, we assessed the outcome of 'complete miscarriage' as very low-quality due to lack of blinding, heterogeneity of the studies, and the small sample size. Findings for the outcome of surgical evacuation were based on low-quality evidence because of high risk of bias in one of the studies and high level of heterogeneity. For the misoprostol versus surgery comparison, the high risk of bias in some included studies, inconsistencies between results across studies, and suspected publication bias were the reasons for downgrading the quality of evidence for the complete miscarriage and surgical evacuation outcomes to very low. We assessed the quality of evidence for unplanned surgical intervention and nausea as low due to the high risk of bias and inconsistencies in the results. We assessed the quality of evidence for women's views, vomiting, and diarrhoea as moderate due to the lack of blinding.

Potential biases in the review process

We attempted to minimise bias by the following; two review authors assessed eligibility for inclusion and two review authors carried out data extraction and assessed risk of bias. Data entry into Review Manager 5 was undertaken by one review author and checked by another (RevMan 2014). However, many of these steps involve subjective assessments and thus may carry some risk of bias.

Agreements and disagreements with other studies or reviews

We are unaware of other reviews on this topic. Our conclusions seem to agree with most of those of the included studies that women can be offered a choice of treatments because differences are small and not of major consequence. Women may have particular preferences as to the adverse effects they wish to try to avoid and this is likely to influence their choice of treatment.

AUTHORS' CONCLUSIONS

Implications for practice

Although it would be critical to have more data, the current evidence suggests there appears to be no major differences, other than avoiding surgery, between misoprostol, expectant care, and surgery in the treatment of incomplete miscarriage for women of less than 13 weeks' gestation. Avoiding surgery has considerable benefits in terms of reducing adverse effects (although these were not fully assessed systematically in the included studies) and is particularly beneficial in low-income countries. We identified some differences in nausea, vomiting, and diarrhoea with the use of misoprostol which can be taken into account when counselling women on the treatment options.

Implications for research

There is an urgent need for studies to assess medical interventions for incomplete miscarriage for women between 13 to 24 weeks' gestation, as currently there are no trials to guide practice. Multicentre trials would seem appropriate to give sufficient size to provide sound evidence.

There is a need for more trials comparing the use of medical treatments, by the various routes, with expectant care and surgery to confirm or refute these findings for women less than 13 weeks' gestation. This should provide more evidence on the effectiveness and adverse effects, so women can be provided with better information in order to support their choices. Future trials should separate women with non-viable pregnancies prior to miscarriage, from those with incomplete miscarriages.

Women's views and quality of life measures should be assessed alongside the clinical outcome in any future trials. These trials should be large enough to provide definitive findings and should assess the important outcomes identified in this review.

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REFERENCES

References to studies included in this review

Bique 2007 *{published data only}*

Bique C, Usta M, Debora B, Chong E, Westheimer E, Winikoff B. Comparison of misoprostol and manual vacuum aspiration for the treatment of incomplete abortion. *International Journal of Gynecology and Obstetrics* 2007;**98** (3):222–6.

Blanchard 2004 *{published data only}*

* Blanchard K, Taneepanichskul S, Kiriwat O, Sirimai K, Svirirojana N, Mavimbela N, et al. Two regimens of misoprostol for treatment of incomplete abortion. *Obstetrics and Gynecology* 2004;**103**(5 Pt 1):860–5.

Phupong V, Taneepanichskul S, Kriengsinyot R, Sriyirojana N, Blanchard K, Winikoff B. Comparative study between single dose 600 mg and repeated dose oral misoprostol for treatment of incomplete abortion. *Contraception* 2004;**70**: 307–11.

Blohm 2005 *{published data only}*

Blohm F, Friden BE, Milsom I, Platz-Christensen JJ, Nielsen S. A randomised double blind trial comparing misoprostol or placebo in the management of early miscarriage. BJOG: an international journal of obstetrics and gynaecology 2005; Vol. 112, issue 8:1090–5.

Chigbu 2012 *{published data only}*

Chigbu B, Onwere S, Aluka C, Kamanu C, Ezenobi O. Is misoprostol a suitable alternative to the surgical evacuation of incomplete abortion in rural South-Eastern Nigeria?. *East African Medical Journal* 2012;**89**(5):172–7.

Clevin 2001 *{published data only}*

Clevin L, Munk T, Hansen TR. Spontaneous abortion. Drug treatment versus surgery [Spontan abort. Medicinsk versus kirurgisk behandling]. *Ugeskrift for Laeger* 2001;**163** (15):2136–9.

Dabash 2010 *{published data only}*

Dabash R, Cherine M, Darwish E, Blum J, Hassanein N, Abdel Daiem T, et al. Bleeding following surgical (MVA) and medical (400 ug sublingual misoprostol) treatment of incomplete abortion. *International Journal of Gynecology and Obstetrics* 2009;**107**(Suppl 2):S150–1.

* Dabash R, Ramadan MC, Darwish E, Hassanein N, Blum J, Winikoff B. A randomized controlled trial of 400-μg sublingual misoprostol versus manual vacuum aspiration for the treatment of incomplete abortion in two Egyptian hospitals. *International Journal of Gynecology and Obstetrics* 2010;**111**(2):131–5.

Ramadan MC. Misoprostol versus MVA for incomplete abortion: results from a randomized controlled trial in Egypt. *International Journal of Gynecology and Obstetrics* 2009;**107**(Suppl 2):S68–9.

Dao 2007 *{published data only}*

Dao B, Blum J, Thieba B, Raghavan S, Ouedraego M, Lankoande J, et al. Is misoprostol a safe, effective and acceptable alternative to manual vacuum aspiration for postabortion care? Results from a randomised trial in Burkina Faso, West Africa. *BJOG: an international journal of obstetrics and gynaecology* 2007;**114**(11):1368–75.

Diop 2009 *{published data only}*

Diop A, Raghavan S, Rakotovao JP, Comendant R, Blumenthal PD, Winikoff B. Two routes of administration for misoprostol in the treatment of incomplete abortion: a randomized clinical trial. *Contraception* 2009;**79**(6): 456–62.

Ganguly 2010 *{published data only}*

Ganguly RP, Mukhopadhyay S, Burman SK, Patra KK, Jha T, Mukherji J. A randomized trial of misoprostol compared with manual vacuum aspiration for early pregnancy failure. *Nepal Journal of Obstetrics and Gynaecology* 2010;**5**(2):8–13.

Montesinos 2011 *{published data only}*

Arellano M, Durocher J, Leon W, Montesinos R, Pena M, Winikoff B. Introduction of misoprostol for incomplete abortion care in Latin America: evidence from Ecuador. *International Journal of Gynecology and Obstetrics* 2009;**107** (Suppl 2):S49.

* Montesinos R, Durocher J, Leon W, Arellano M, Pena M, Pinto E, et al. Oral misoprostol for the management of

incomplete abortion in Ecuador. *International Journal of Gynecology and Obstetrics* 2011;**115**(2):135–9.

Moodliar 2005 *{published data only}*

Bagratee J, Regan L, Khullar V, Moodley J, Connolly C. Does the volume of retained products of conception and hormonal parameters influence the success of conservative methods of management of first trimester miscarriage?. *International Journal of Gynecology and Obstetrics* 2009;**107** (Suppl 2):S116.

* Moodliar S, Bagratee JS, Moodley J. Medical vs. surgical evacuation of first-trimester spontaneous abortion. *International Journal of Gynecology and Obstetrics* 2005;**91**: 21–6.

Ngoc 2005 *{published data only}*

Nguyen TNN, Blum J, Durocher J, Quan TTV, Winikoff B. A randomized controlled study comparing 600 versus 1, 200 micrograms oral misoprostol for medical management of incomplete abortion. Contraception 2005; Vol. 72, issue 6:438–42.

Niinimaki 2006 *{published data only}*

* Niinimaki M, Jouppila P, Martikainen H, Talvensaari-Mattila A. A randomized study comparing efficacy and patient satisfaction in medical or surgical treatment of miscarriage. *Fertility and Sterility* 2006;**86**(2):367–72.

Niinimaki M, Karinen P, Hartikainen AL, Pouta A. Treating miscarriages: a randomised study of cost-effectiveness in medical or surgical choice. *BJOG: an international journal of obstetrics and gynaecology* 2009;**116**(7):984–90.

Pang 2001 *{published data only}*

* Pang MW, Chung T. Incomplete miscarriage: a randomized controlled trial comparing oral with vaginal misoprostol for medical evacuation. *Human Reproduction* 2001;**16**(11):2283–7.

Pang SMW, Chung TKH. A randomized clinical trial comparing oral and vaginal misoprostol for medical evacuation of spontaneous abortion [abstract]. XVI FIGO World Congress of Obstetrics and Gynecology (Book 3); 2000 Sept 3-8; Washington DC, USA. 2000:69.

Paritakul 2010 *{published data only}*

Paritakul P, Phupong V. Comparative study between oral and sublingual 600 μg misoprostol for the treatment of incomplete abortion. *Journal of Obstetrics and Gynaecology Research* 2010;**36**(5):978–83.

Patua 2013 *{published data only}*

Patua B, Dasgupta M, Bhattacharyya SK, Bhattacharya S, Hasan SH, Saha S. An approach to evaluate the efficacy of vaginal misoprostol administered for a rapid management of first trimester spontaneous onset incomplete abortion, in comparison to surgical curettage. *Archives of Gynecology and Obstetrics* 2013;**288**(6):1243–8.

Sahin 2001 *{published data only}*

Sahin HG, Sahin HA, Kocer M. Randomized outpatient clinical trial of medical evacuation and surgical curettage in incomplete miscarriage. *European Journal of Contraception & Reproductive Health Care* 2001;**6**(3):141–4.

Shelley 2005 *{published data only}*

Shelley JM, Healy D, Grover S. A randomised trial of surgical, medical and expectant management of first trimester spontaneous miscarriage. Australian and New Zealand Journal of Obstetrics and Gynaecology 2005; Vol. 45:122–7.

Shochet 2012 *{published data only}*

Shochet T, Diop A, Gaye A, Nayama M, Sall AB, Bukola F, et al. Sublingual misoprostol versus standard surgical care for treatment of incomplete abortion in five sub-Saharan African countries. *BMC Pregnancy and Childbirth* 2012;**12**: 127.

Shwekerela 2007 *{published data only}*

Shwekerela B, Kalumuna R, Kipingili R, Mashaka N, Westheimer E, Clark W, et al. Misoprostol for treatment of incomplete abortion at the regional hospital level: results from Tanzania. *BJOG: an international journal of obstetrics and gynaecology* 2007;**114**(11):1363–7.

Taylor 2011 *{published data only}*

Taylor J, Diop A, Blum J, Dolo O, Winikoff B. Oral misoprostol as an alternative to surgical management for incomplete abortion in Ghana. *International Journal of Gynecology and Obstetrics* 2011;**112**(1):40–4.

Trinder 2006 *{published data only}*

Petrou S, Trinder J, Brocklehurst P, Smith L. Economic evaluation of alternative management methods of first-trimester miscarriage based on results from the MIST trial. *BJOG: an international journal of obstetrics and gynaecology* 2006;**113**(8):879–89.

Smith L. Extension to: randomised controlled trial of expectant, medical and surgical management of early miscarriage. www.refer.nhs.uk (accessed 7 March 2006).

Smith LF, Frost J, Levitas R, Bradley H, Garcia J. Women's experiences of three early miscarriage management options: a qualitative study. *British Journal of General Practice* 2006; **56**(524):198–205.

Smith LFP, Ewings PD, Quinlan C. Incidence of pregnancy after expectant, medical, or surgical management of spontaneous first trimester miscarriage: long term follow-up of miscarriage treatment (MIST) randomised controlled trial. *BMJ* 2009;**339**(1766):b3827.

* Trinder J, Brocklehurst P, Porter R, Read M, Vyas S, Smith L. Management of miscarriage: expectant, medical, or surgical? Results of randomised controlled trial (miscarriage treatment (MIST) trial). *BMJ* 2006;**332**(7552):1235–40.

Weeks 2005 *{published data only}*

Weeks A, Alia G, Blum J, Blanchard K, Winikoff B. A randomised trial of oral misoprostol (600 mcg) versus manual vacuum aspiration in the treatment of incomplete miscarriage in Kampala, Uganda. 30th British Congress of Obstetrics and Gynaecology; 2004 July 7-9; Glasgow, UK. 2004:27.

* Weeks A, Alia G, Blum J, Winikoff B, Ekwaru P, Durocher J, et al. A randomized trial of misoprostol compared with manual vacuum aspiration for incomplete abortion. *Obstetrics and Gynecology* 2005;**106**(3):540–7.

Zhang 2005 *{published data only}*

Chen BA, Reeves MF, Creinin MD, Gilles JM, Barnhart K, Westhoff C, et al. Misoprostol for treatment of early pregnancy failure in women with previous uterine surgery. *American Journal of Obstetrics and Gynecology* 2008;**198**(6): 626.e1–5.

Creinin MD, Huang X, Westhoff C, Barnhart K, Gilles JM, Zhang J, et al. Factors related to successful misoprostol treatment for early pregnancy failure. *Obstetrics and Gynecology* 2006;**107**(4):901–7.

Harwood B, Nansel T, National Institute of Child Health and Human Development Management of Early Pregnancy Failure Trial. Quality of life and acceptability of medical versus surgical management of early pregnancy failure. *BJOG: an international journal of obstetrics and gynaecology* 2008;**115**(4):501–8.

Reeves MF, Lohr PA, Harwood B, Creinin MD. Sonographic findings after misoprostol or vacuum aspiration for early pregnancy failure. *Contraception* 2006;**74**(2):182.

Reeves MF, Lohr PA, Harwood BJ, Creinin MD. Ultrasonographic endometrial thickness after medical and surgical management of early pregnancy failure. *Obstetrics and Gynecology* 2008;**111**(1):106–12.

Robledo C, Zhang J, Troendle J, Barnhart K, Creinin MD, Westhoff C, et al. Clinical indicators for success of misoprostol treatment after early pregnancy failure. *International Journal of Gynecology and Obstetrics* 2007;**99** (1):46–51.

Zhang J, Gilles J, Barnhart K, Creinin M, Westhoff C, Frederick MM. Medical management with misoprostol for early pregnancy failure: a multicenter, randomized equivalence trial [abstract]. *Fertility and Sterility* 2004;**82 Suppl 2**:S53–4.

* Zhang J, Gilles JM, Barnhart K, Creinin MD, Westhoff C, Frederick MM, et al. A comparison of medical management with misoprostol and surgical management for early pregnancy failure. *New England Journal of Medicine* 2005; **353**(8):761–9.

References to studies excluded from this review

Abdel 1997 *{published data only}*

Abdel Fattah IH. PGE1 analogue for the induction of midtrimester abortion in cases of intrauterine fetal death. *Acta Obstetricia et Gynecologica Scandinavica Supplement* 1997;**76**(167):26.

Abd-El-Maeboud 2012 *{published data only}*

Abd-El-Maeboud KH, Ghazy A, Ibrahim A, Hassan N, El-Bohoty A, Gamal-El-Din I. Vaginal acidity enhancement with a 3% acetic acid gel prior to misoprostol treatment for pregnancy termination in the midtrimester. *International Journal of Gynecology and Obstetrics* 2012;**119**(3):248–52.

Al-Bdour 2007 *{published data only}*

Al-Bdour AN, Akasheh H, Al-Jayousi T. Missed abortion: termination using single-dose versus two doses of vaginal misoprostol tablets. *Pakistan Journal of Medical Sciences* 2007;**23**(6):920–3.

Al Inizi 2003 *{published data only}*

Al Inizi SA, Ezimokhai M. Vaginal misoprostol versus dinoprostone for the management of missed abortion. *International Journal of Gynecology and Obstetrics* 2003;**83**: 73–4.

Almog 2005 *{published data only}*

Almog B, Levin I, Winkler N, Fainaru O, Pauzner D, Lessing JB, et al. The contribution of laminaria placement for cervical ripening in second trimester termination of pregnancy induced by intra-amniotic injection of prostaglandin f(2)alpha followed by concentrated oxytocin infusion. *European Journal of Obstetrics, Gynecology, and Reproductive Biology* 2005;**118**:32–5.

Altaf 2006 *{published data only}*

Altaf F, Sultana N, Iqbal N. Therapeutic abortions; efficacy of intra-vaginal misoprostol in comparison to extra amniotically administered prostaglandin f2a. *Professional Medical Journal* 2006;**13**(3):417–22.

Amjad 1999 *{published data only}*

Amjad T, Akhtar S. Termination of pregnancy with foetal death in second trimester: Foley's catheter versus extra amniotic prostaglandins. *Journal of the College of Physicians and Surgeons Pakistan* 1999;**9**:403–5.

Anderman 2000 *{published data only}*

Anderman S, Jaschevatzky OE, Ballas S. Comparison between a double balloon device and the foley catheter in extraamniotic prostaglandin F2a infusion for termination of midtrimester missed abortion [abstract]. XVI FIGO World Congress of Obstetrics and& Gynecology (Book 2); 2000 Sept 3-8; Washington DC, USA. 2000:161.

Anderson 2009 *{published data only}*

Anderson J, Gouk E, Young L, Turnbull L, Sayeed G, Elattar A, et al. A randomised controlled trial of oral versus vaginal misoprostol for medical management of early fetal demise. *International Journal of Gynecology and Obstetrics* 2009;**107**(Suppl 2):S533.

Ara 2009 *{published data only}*

Ara G, Nargis S, Khatun R, Saha A. Vaginal misoprostol as a medical management in early pregnancy loss. *International Journal of Gynecology and Obstetrics* 2009;**107**(Suppl 2): S533–4.

Autry 1999 *{published data only}*

Autry A, Jacobson G, Sandhu R, Isbill K. Medical management of non-viable early first trimester pregnancy. International Journal of Gynecology and Obstetrics 1999; Vol. 67, issue 1:9–13.

Avila-Vergara 1997 *{published data only}*

Avila-Vergara MA, Morgan-Ortiz F, Fragoza-Sosa O, Haro-Garcia L. Cervical labor induction with prostaglandin E2 in patients with fetal death [Maduracion cervical con prostaglandina E2 en pacientes con feto muerto]. *Ginecologia y Obstetricia de Mexico* 1997;**65**:155–8.

Ayudhaya 2006 *{published data only}*

Ayudhaya OP, Herabutya Y, Chanrachakul B, Ayuthaya NI, O-Prasertsawat P. A comparison of the efficacy of sublingual

and oral misoprostol 400 microgram in the management of early pregnancy failure: a randomized controlled trial. *Journal of the Medical Association of Thailand* 2006;**89** (Suppl 4):S5–S10.

Azra 2007 ***{published data only}***
Azra B, Shakeel S, Nilofer M. A comparison of two protocols of intra vaginal misoprostol for second trimester medical termination of pregnancy. *Pakistan Armed Forces Medical Journal* 2007;**57**(1):61–5.

Bagratee 2004 ***{published data only}***
Bagratee JS, Khullar V, Regan L, Moodley J, Kagoro H. A randomized controlled trial comparing medical and expectant management of first trimester miscarriage. *Human Reproduction* 2004;**19**(2):266–71.

Bani-Irshaid 2006 ***{published data only}***
Bani-Irshaid I, Athamneh TZ, Bani-Khaled D, Al-Momani M, Dahamsheh H. Termination of second and early third trimester pregnancy: comparison of 3 methods. *Eastern Mediterranean Health Journal* 2006;**12**(5):605–9.

Bebbington 2002 ***{published data only}***
Bebbington MW, Kent N, Lim K, Gagnon A, Delisle MF, Tessier F, et al. A randomized controlled trial comparing two protocols for the use of misoprostol in midtrimester pregnancy termination. *American Journal of Obstetrics and Gynecology* 2002;**187**(4):853–7.

Behrashi 2008 ***{published data only}***
Behrashi M. Comparison between the oral and vaginal misoprostol effects on pregnancy termination in second trimester. en.search.irct.ir/view/90 Date first received: 27 September 2008.
* Behrashi M, Mahdian M. Vaginal versus oral misoprostol for second-trimester pregnancy termination: a randomized trial. *Pakistan Journal of Biological Sciences* 2008;**11**(21): 2505–8.

Ben-Meir 2009 ***{published data only}***
Ben-Meir A, Erez Y, Feigenberg T, Hamani Y, Laufer N, Rojansky N. Mifepristone followed by high-dose oxytocin drip for second-trimester abortion: a randomized, double-blind, placebo-controlled, pilot study. *Journal of Reproductive Medicine* 2009;**54**(8):511–6.

Biswas 2007 ***{published data only}***
Biswas SC, Dey R, Jana R, Chattopadhyay N. Comparative study of intravaginal misoprostol and extra amniotic ethacridine lactate instillation for mid trimester pregnancy termination. *Journal of Obstetrics and Gynaecology of India* 2007;**57**(3):211–3.

Cabrol 1990 ***{published data only}***
Cabrol D, Dubois C, Cronje H, Gonnet JM, Guillot M, Maria B, et al. Induction of labor with mifepristone (RU 486) in intrauterine fetal death. *American Journal of Obstetrics and Gynecology* 1990;**163**:540–2.

Caliskan 2005 ***{published data only}***
Caliskan E, Dilbaz S, Doger E, Ozeren S, Dilbaz B. Randomized comparison of 3 misoprostol protocols for abortion induction at 13-20 weeks of gestation. *Journal of Reproductive Medicine* 2005;**50**(3):173–80.

Caliskan 2009 ***{published data only}***
Caliskan E, Doger E, Cakiroglu Y, Corakci A, Yucesoy I. Sublingual misoprostol 100 microgram versus 200 microgram for second trimester abortion: a randomised trial. *European Journal of Contraception & Reproductive Health Care* 2009;**14**(1):55–60.

Chittacharoen 2003 ***{published data only}***
Chittacharoen A, Herabutya Y, Punyavachira P. A randomized trial of oral and vaginal misoprostol to manage delivery in cases of fetal death. *Obstetrics and Gynecology* 2003;**101**:70–3.

Chung 1999 ***{published data only}***
Chung TKH, Cheung LP, Haines CJ. Spontaneous abortion: A randomized controlled trial of misoprostol versus routine surgical evacuation. *Acta Obstetricia et Gynecologica Scandinavica* 1997;**76**(167):72.
Chung TKH, Cheung LP, Lee DTS, Haines CJ. Spontaneous abortion: a randomized controlled trial of misoprostol versus routine uterine curettage. *British Journal of Obstetrics and Gynaecology* 1998;**105 Suppl 17**:127.
Chung TKH, Lee DTC. A randomised controlled clinical trial involving women who have aborted spontaneously: the health, social and operational cost outcomes of conservative and routine management protocols. Personal communication 1998.
* Chung TKH, Lee DTS, Cheung LP, Haines CJ, Chang AMZ. Spontaneous abortion: a randomised controlled trial comparing surgical evacuation with conservative management using misoprostol. *Fertility and Sterility* 1999; **71**(6):1054–9.
Lee DTS, Cheung LP, Haines CJ, Chan KPM, Chung TKH. A comparison of the psychologic impact and client satisfaction of surgical treatment with medical treatment of spontaneous abortion: a randomized controlled trial. *American Journal of Obstetrics and Gynecology* 2001;**185**: 953–8.
Tam WH, Lau WC, Cheung LP, Yuen PM, Chung TK. Intrauterine adhesions after conservative and surgical management of spontaneous abortion. *Journal of the American Association of Gynecologic Laparoscopists* 2002;**9**(2): 182–5.
Tam WH, Tsui MH, Lok IH, Yip SK, Yuen PM, Chung TK. Long-term reproductive outcome subsequent to medical versus surgical treatment for miscarriage. *Human Reproduction* 2005;**20**(12):3355–9.

Cleeve 2015 ***{published data only}***
Cleeve A, Byamugisha J, Gemzell-Danielsson K, Mbona Tumwesigye N, Atuhairwe S, Faxelid E, et al. Women's acceptability of misoprostol treatment for incomplete abortion by midwives and physicians - a randomized controlled equivalence trial at district level, Uganda. *International Journal of Gynecology and Obstetrics* 2015;**131** (Suppl 5):E295.

Creinin 1997 ***{published data only}***
Creinin MD, Moyer R, Guido R. Misoprostol for medical evacuation of early pregnancy failure. *Obstetrics and Gynecology* 1997;**89**:768–72.

David 2003 *{published data only}*
David M, Chen FCK, Lichtenegger W. NO-donor nitroglycerin versus the prostaglandin gemeprost for cervical ripening in first trimester missed abortion. *International Journal of Gynecology and Obstetrics* 2003;**83**:71–2.

David 2005 *{published data only}*
David M, Chen FCK. Comparison of isosorbide mononitrate (Mono Mack) and misoprostol (Cytotec) for cervical ripening in the first trimester missed abortion. *Archives of Gynecology and Obstetrics* 2005;**273**(3):144–5.

de Jonge 1995 *{published data only}*
de Jonge ET, Makin JD, Manefeldt E, De Wet GH, Pattinson RC. Randomised clinical trial of medical evacuation and surgical curettage for incomplete miscarriage. *BMJ* 1995;**311**(7006):662.

Demetroulis 2001 *{published data only}*
* Demetroulis C, Saridogan E, Kunde D, Naftalin AA. A prospective randomized control trial comparing medical and surgical treatment for early pregnancy failure. *Human Reproduction* 2001;**16**(2):365–9.
Demetroulis C, Saridogan E, Kunde D, Naftalin AA. A prospective randomized control trial comparing medical and surgical treatment for early pregnancy failure [abstract]. XVI FIGO World Congress of Obstetrics and Gynecology (Book 3); 2000 Sept 3-8; Washington DC, USA. 2000:69.

Dickinson 1998 *{published data only}*
Dickinson JE, Godfrey M, Evans SF. Efficacy of intravaginal misoprostol in second-trimester pregnancy termination: a randomized controlled trial. *Journal of Maternal-Fetal Medicine* 1998;**7**:115–9.

Dickinson 2002 *{published data only}*
Dickinson JE, Evans SF. The optimization of intravaginal misoprostol dosing schedules in second-trimester pregnancy termination. American Journal of Obstetrics and Gynecology 2002; Vol. 186, issue 3:470–4.

Dickinson 2003 *{published data only}*
Dickinson JE, Evans SF. A comparison of oral misoprostol with vaginal misoprostol administration in second-trimester pregnancy termination for fetal abnormality. *Obstetrics and Gynecology* 2003;**101**:1294–9.

Egarter 1995 *{published data only}*
Egarter C, Lederhilger J, Kurz C, Karas H, Reisenberger K. Gemeprost for first trimester missed abortion. *Archives of Gynecology and Obstetrics* 1995;**256**(1):29–32.

Elhassan 2008 *{published data only}*
Elhassan EM, Abubaker MS, Adam I. Sublingual compared with oral and vaginal misoprostol for termination of pregnancy with second-trimester fetal demise. *International Journal of Gynecology and Obstetrics* 2008;**100**(1):82–3.

Eng 1997 *{published data only}*
Eng NS, Guan AC. Comparative study of intravaginal misoprostol with gemeprost as an abortifacient in second trimester missed abortion. *Australian and New Zealand Journal of Obstetrics and Gynaecology* 1997;**37**(3):331–4.

Eppel 2005 *{published data only}*
Eppel W, Facchinetti F, Schleussner E, Piccinini F, Pizzi C, Gruber DM, et al. Second trimester abortion using isosorbide mononitrate in addition to gemeprost compared with gemeprost alone: a double-blind randomized, placebo-controlled multicenter trial. *American Journal of Obstetrics and Gynecology* 2005;**192**:856–61.

Fadalla 2004 *{published data only}*
Fadalla F, Mirghani OA, Adam I. Oral misoprostol vs. vaginal misoprostol for termination of pregnancy with intrauterine fetal demise in the second-trimester. *International Journal of Gynecology and Obstetrics* 2004;**86**: 52–3.

Fang 2009 *{published data only}*
Fang AH, Chen QF, Zheng W, Li YH, Chen RY. Termination of missed abortion in a combined procedure: a randomized controlled trial. *Journal of Reproduction and Contraception* 2009;**20**(1):45–9.

Feldman 2003 *{published data only}*
Feldman DM, Borgida AF, Rodis JF, Leo MV, Campbell WA. A randomized comparison of two regimens of misoprostol for second-trimester pregnancy termination. American Journal of Obstetrics and Gynecology 2003; Vol. 189:710–3.

Fiala 2005 *{published data only}*
Fiala C, Swahn ML, Stephansson O, Gemzell-Danielsson K. The effect of non-steroidal anti-inflammatory drugs on medical abortion with mifepristone and misoprostol at 13-22 weeks gestation. Human Reproduction 2005; Vol. 20, issue 11:3072–7.

Gazvani 2000 *{published data only}*
Gazvani R, Templeton A. A pilot study for the use of manual vacuum aspiration in early pregnancy loss. *Journal of Obstetrics and Gynaecology* 2000;**20**(1):105.

Ghorab 1998 *{published data only}*
Ghorab MN, El Helw BA. Second-trimester termination of pregnancy by extra-amniotic prostaglandin F2alpha or endocervical misoprostol A comparative study. *Acta Obstetricia et Gynecologica Scandinavica* 1998;**77**:429–32.

Gilles 2004 *{published data only}*
Barnhart KT, Bader T, Huang X, Frederick MM, Timbers KA, Zhang JJ. Hormone pattern after misoprostol administration for a nonviable first-trimester gestation. *Fertility and Sterility* 2004;**81**(4):1099–105.
Creinin MD, Harwood B, Guido RS, Fox MC, Zhang J, NICHD Management of Early Pregnancy Failure Trial. Endometrial thickness after misoprostol use for early pregnancy failure. *International Journal of Gynecology and Obstetrics* 2004;**86**(1):22–6.
Davis AR, Robilotto CM, Westhoff CL, Forman S, Zhang J, NICHD Management of Early Pregnancy Failure Trial. Bleeding patterns after vaginal misoprostol for treatment of early pregnancy failure. *Human Reproduction* 2004;**19**(7): 1655–8.
Gilles J, Creinin MM, Barnhart KT, Westhoff C, Frederick MM, Zang J. Wet versus dry intravaginal misoprostol

application for treatment of early pregnancy failure [abstract]. *Fertility and Sterility* 2002;**78**(3 Suppl 1):S64–5.
* Gilles JM, Creinin MD, Barnhart K, Westhoff C, Frederick MM, Zhang J. A randomized trial of saline solution-moistened misoprostol versus dry misoprostol for first-trimester pregnancy failure. American Journal of Obstetrics and Gynecology 2004; Vol. 190:389–94.

Gonzalez 2001 *{published data only}*
Gonzalez JA, Carlan SJ, Alverson MW. Outpatient second trimester pregnancy termination. *Contraception* 2001;**63**(2):89–93.

Graziosi 2004 *{published data only}*
Graziosi G, Bruinse HW, Reuwer PJH, Teteringen O, Mol BJW. Fertility outcome after a randomized trial comparing curettage with misoprostol for treatment of early pregnancy failure. *Human Reproduction* 2005;**20**:1749–50.
Graziosi GC, van der Steeg JW, Reuwer PH, Drogtrop AP, Bruinse HW, Mol BW. Economic evaluation of misoprostol in the treatment of early pregnancy failure compared to curettage after an expectant management. *Human Reproduction* 2005;**20**(4):1067–71.
Graziosi GCM, Bruinse HW, Reuwer PJH, van Kessel PH, Westerweel PE, Mol BW. Misoprostol versus curettage in women with early pregnancy failure: impact on women's health-related quality life. A randomized controlled trial. *Human Reproduction* 2005;**20**(8):2340–7.
* Graziosi GCM, Mol BWJ, Reuwer PJH, Drogtrop A, Bruinse HW. Misoprostol versus curettage in women with early pregnancy failure after initial expectant management: a randomized trial. *Human Reproduction* 2004;**19**(8):1894–9.

Grimes 2005 *{published data only}*
Grimes DA, Smith MS, Witham AD. Mifepristone and misoprostol versus dilation and evacuation for midtrimester abortion: a pilot randomised controlled trial. *BJOG: an international journal of obstetrics and gynaecology* 2005;**111**:148–53.

Gronlund 2002 *{published data only}*
Gronlund A, Gronlund L, Clevin L, Andersen B, Palmgren N, Lidegaard O. Management of missed abortion: comparison of medical treatment with either mifepristone + misoprostol or misoprostol alone with surgical evacuation. A multi-center trial in Copenhagen county, Denmark. *Acta Obstetricia et Gynecologica Scandinavica* 2002;**81**:1060–5.

Guix 2005 *{published data only}*
Guix C, Palacio M, Figueras F, Bennasar M, Zamora L, Coll O, et al. Efficacy of two regimens of misoprostol for early second-trimester pregnancy termination. *Fetal Diagnosis and Therapy* 2005;**20**(6):544–8.

Hassan 2007 *{published data only}*
Hassan FI, Mostapha MK, Sattar MA, Marouf E, Azim SA. Oral versus rectal route of misoprostol administration: a randomized controlled trial. *Middle East Fertility Society Journal* 2007;**12**(1):53–6.

Hausler 1997 *{published data only}*
Hausler MCH, Koroschetz F, Tamussino K, Walcher W. Is a curettage after spontaneous abortion still relevant? [Ist eine currettage nach abortus completus noch zeitgemals?]. *Geburtshilfe und Frauenheilkunde* 1997;**57**:396–9.

Heard 2002 *{published data only}*
Heard MJ, Stewart GM, Buster JE, Carson SA, Miller HJ. Outpatient management of missed abortion with vaginal misoprostol [abstract]. *Obstetrics and Gynecology* 2002;**99**(4 Suppl):20S.

Herabutya 1997a *{published data only}*
Herabutya Y, O-Prasertsawat P. Misoprostol in the management of missed abortion. *International Journal of Gynecology and Obstetrics* 1997;**56**(3):263–6.

Herabutya 1997b *{published data only}*
Herabutya Y, O-Prasertsawat P. A comparison of intravaginal misoprostol with intracervical prostaglandin E2 gel for the management of dead fetus in utero. Thai Journal of Obstetrics and Gynaecology 1997; Vol. 9, issue 2:95–8.

Herabutya 2005 *{published data only}*
Herabutya Y, Chanrachakul B, Punyavachira P. A randomised controlled trial of 6 and 12 hourly administration of vaginal misoprostol for second trimester pregnancy termination. *BJOG: an international journal of obstetrics and gynaecology* 2005;**112**(9):1297–301.

Hernandez-Valencia 2003 *{published data only}*
Hernandez-Valencia M. Cervical ripening with prostaglandin E1: how an ambulatory method decreases the hospital stay in abortus with intrauterine fetal demise. *Fetal Diagnosis and Therapy* 2003;**18**(1):54–8.

Hidar 2001 *{published data only}*
Hidar S, Fekih M, Chaieb A, Bibi M, Mellouli R, Khairi H. Oxytocin and misoprostol administered intravaginally for termination of pregnancy at 13 to 29 weeks of amenorrhea A prospective randomized trial [Apport de l'association d'ocytocine au misoprostol administre en intravaginal au cours des interruptions de grossesses entre 13 et 29 semaines d'amenorrhee. Essai clinique prospectif randomise]. *Journal de Gynecologie, Obstetrique et Biologie de la Reproduction* 2001;**30**(5):439–43.

Hidar 2005 *{published data only}*
Hidar S, Bouddebous M, Chaieb A, Jerbi M, Bibi M, Khairi H. Randomized controlled trial of vaginal misoprostol versus vaginal misoprostol and isosorbide dinitrate for termination of pregnancy at 13-29 weeks. *Archives of Gynecology and Obstetrics* 2005;**273**(3):157–60.

Hill 1991 *{published data only}*
Hill NCW, Selinger M, Ferguson J, MacKenzie IZ. Management of intra-uterine fetal death with vaginal administration of gemeprost or prostaglandin E2: a random allocation controlled trial. *Journal of Obstetrics and Gynaecology* 1991;**11**:422–6.

Hinshaw 1997 *{published data only}*
Davis AR, Hendlish SK, Westhoff C, Frederick MM, Zhang J, Gilles JM, et al. Bleeding patterns after misoprostol vs

surgical treatment of early pregnancy failure: results from a randomized trial. *American Journal of Obstetrics and Gynecology* 2007;**196**(1):31.
Henshaw RC, Hinshaw K, Smith NC, Templeton AA. The medical management of miscarriage. Fertility Society of Australia/Australasian Gynaecological Endoscopy Society; 1995 November 19-25; Melbourne, Australia. 1995: FSA75.
* Hinshaw HKS. Medical management of miscarriage. In: Grundzinkas JG editor(s). *Problems in Early Pregnancy - Advances in Diagnosis and Management*. London: RCOG, 1997.
Hinshaw K, Rispin R, Henshaw R, Smith N, Templeton A. Medical versus surgical uterine evacuation in first trimester miscarriage: a prospective, pragmatic randomised trial. 27th British Congress of Obstetrics and Gynaecology; 1995 July 4-7; Dublin, Ireland. 1995:4.
Hinshaw K, Rispin R, Smith N, Templeton A. Medical vs surgical management in first trimester miscarriage: a prospective, pragmatic random allocation trial. *Journal of Obstetrics and Gynaecology* 1993;**13**(5):404–5.
Hughes J, Ryan M, Hinshaw K, Henshaw R, Rispin R, Templeton A. The costs of treating miscarriage: a comparison of medical and surgical management. *British Journal of Obstetrics and Gynaecology* 1996;**103**(12): 1217–21.
Rispin R, Hinshaw K, Henshaw R, Smith N, Templeton A. New aspects of care in the management of miscarriage. Research in Midwifery Conference; 1993 Sept 14; Birmingham, UK. 1993.

Hogg 2000 ***{published data only}***
Hogg B, Owen J. Laminaria versus extraamniotic saline infusion (EASI) for cervical ripening and mid-trimester labor induction [abstract]. *American Journal of Obstetrics and Gynecology* 2000;**182**(1 Pt 2):S135.

Hombalegowda 2015 ***{published data only}***
Hombalegowda RB, Samapthkumar S, Vana H, Jogi P, Ramaiah R. A randomized controlled trial comparing different doses of intravaginal misoprostol for early pregnancy failure. *Contraception* 2015;**92**(4):364–5.

Igogo 2015 ***{published data only}***
Igogo P, Karanja J, Kamau K, Tamooh H. Use of misoprostol for incomplete abortion in resource-poor settings. *Contraception* 2015;**92**(4):370.

IRCT138902053797N1 ***{published data only}***
IRCT138902053797N1. Comparing the effects of multiple doses of misoprostol with single dose of misoprostol plus oxytocin in induction of second trimester abortion [Comparing effects of different doses of misoprostol in induction of second trimester abortion]. irct.ir/138902053797N1 (first received 12 June 2010).

Islam 2006 ***{published data only}***
Islam A, Abbasi AN, Sarwar I. Use of Foley's catheter and prostaglandin F-2 alpha in second trimester termination of pregnancy. *Journal of Ayub Medical College, Abbottabad* 2006;**18**(3):35–9.

Jabir 2009 ***{published data only}***
Jabir M, Smeet R. Comparison of oral and vaginal misoprostol for cervical ripening before evacuation of first trimester missed miscarriage. *International Journal of Gynecology and Obstetrics* 2009;**107**(Suppl 2):S209.
* Jabir M, Smeet RI. Comparison of oral and vaginal misoprostol for cervical ripening before evacuation of first trimester missed miscarriage. *Saudi Medical Journal* 2009; **30**(1):82–7.

Jain 1994 ***{published data only}***
Jain JK, Mishell DR. A comparison of intravaginal misoprostol with prostaglandin E2 for termination of second-trimester pregnancy. *New England Journal of Medicine* 1994;**331**:290–3.

Jain 1996 ***{published data only}***
Jain JK, Mishell DR. A comparison of misoprostol with and without laminaria tents for induction of second-trimester abortion. *American Journal of Obstetrics and Gynecology* 1996;**175**:173–7.

Jain 1999 ***{published data only}***
Jain JK, Mishell DR. A comparison of two dosing regimens of intravaginal misoprostol for second-trimester pregnancy termination. *Obstetrics and Gynecology* 1999;**93**:571–5.

Johnson 1997 ***{published data only}***
Johnson N, Priestnall M, Marsay T, Ballard P, Watters J. A randomised trial evaluating pain and bleeding after a first trimester miscarriage treated surgically or medically. *European Journal of Obstetrics, Gynecology, and Reproductive Biology* 1997;**72**(2):213–5.

Kaluaarachchi 2015 ***{published data only}***
Kaluaarachchi A, Kopalakrishnan M. Surgical, medical or expectant management of first trimester miscarriage and its implications on clinical and psychological outcomes - a randomized controlled trial. *Sri Lanka Journal of Obstetrics and Gynaecology* 2015;**37**(Suppl 1):17.

Kanhai 1989 ***{published data only}***
* Kanhai HHH, Keirse MJNC. Induction of labour after fetal death: a randomized controlled trial of two prostaglandin regimens. *British Journal of Obstetrics and Gynaecology* 1989;**96**:1400–4.
Kanhai HHH, Keirse MJNC. Intravenous administration of sulprostone for the induction of labour after fetal death: a randomized comparison of two dose schedules. 12th FIGO World Congress of Gynecology and Obstetrics; 1988 October 23-28; Brazil. 1988:201–2.
Kanhai HHH, Keirse MJNC. Intravenous administration of sulprostone for the induction of labour after fetal death: a randomized comparison of two dose schedules. First European Congress on Prostaglandins in Reproduction; 1988 July 6-9; Vienna, Austria. 1988:45.

Kapp 2007 ***{published data only}***
Kapp N, Todd CS, Yadgarova KT, Alibayeva G, Nazarova D, Loza O, et al. A randomized comparison of misoprostol to intrauterine instillation of hypertonic saline plus a prostaglandin F2alpha analogue for second-trimester

induction termination in Uzbekistan. *Contraception* 2007; **76**(6):461–6.

Kara 1999 *{published data only}*
Kara M, Ozden S, Eroglu M, Cetin A, Arioglu P. Comparison of misoprostol and dinoproston administration for the induction of labour in second trimester pregnancies in cases of intrauterine fetal loss. *Italian Journal of Gynaecology and Obstetrics* 1999;**11**:13–6.

Klingberg 2015 *{published data only}*
Klingberg-Allvin M, Cleeve A, Atuhairwe S, Mbona Tumwesigye N, Faxelid E, Byamugisha J, et al. Comparison of treatment of incomplete abortion with misoprostol by physicians and midwives at district level in Uganda: a randomised controlled equivalence trial. *International Journal of Gynecology and Obstetrics* 2015;**131**(Suppl 5):E86.

Klingberg-Allvin 2015 *{published data only}*
Klingberg-Allvin M, Cleeve A, Atuhairwe S, Tumwesigye NM, Faxelid E, Byamugisha J, et al. Comparison of treatment of incomplete abortion with misoprostol by physicians and midwives at district level in Uganda: a randomised controlled equivalence trial. *Lancet* 2015;**385**(9985):2392–8.

Kong 2013 *{published data only}*
Kong GW, Lok IH, Yiu AK, Hui AS, Lai BP, Chung TK. Clinical and psychological impact after surgical, medical or expectant management of first-trimester miscarriage - a randomised controlled trial. *Australian & New Zealand Journal of Obstetrics & Gynaecology* 2013;**53**(2):170–7.

Kovavisarach 2002 *{published data only}*
Kovavisarach E, Sathapanachai U. Intravaginal 400 micrograms misoprostol for pregnancy termination in cases of blighted ovum: a randomised controlled trial. *Australian & New Zealand Journal of Obstetrics & Gynaecology* 2002;**42**(2):161–3.

Kovavisarach 2005 *{published data only}*
Kovavisarach E, Jamnansiri C. Intravaginal misoprostol 600 ug and 800 ug for the treatment of early pregnancy failure. *International Journal of Gynecology and Obstetrics* 2005;**90**(3):208–12.

Kushwah 2009 *{published data only}*
Kushwah B, Singh A. Sublingual versus oral misoprostol for uterine evacuation following early pregnancy failure. *International Journal of Gynecology and Obstetrics* 2009;**106**(1):43–5.

Kushwah 2011 *{published data only}*
Kushwah DS, Kushwah B, Salman MT, Verma VK. Acceptability and safety profile of oral and sublingual misoprostol for uterine evacuation following early fetal demise. *Indian Journal of Pharmacology* 2011;**43**(3):306–10.

Lelaidier 1993 *{published data only}*
Lelaidier C, Baton-Saint-Mleux C, Fernandez H, Bourget P, Frydman R. Mifepristone (RU486) induces embryo expulsion in first trimester non-developing pregnancies: a prospective randomized trial. *Human Reproduction* 1993;**8**(3):492–5.

Lippert 1978 *{published data only}*
Lippert TH, Luthi A. Induction of labour with prostaglandin E2 gel in cases of intrauterine fetal death. *Prostaglandins* 1978;**15**:533–42.

Lister 2005 *{published data only}*
Lister MS, Shaffer LET, Bell JG, Lutter KQ, Moorma KH. Randomized, double-blind, placebo-controlled trial of vaginal misoprostol for management of early pregnancy failures. *American Journal of Obstetrics and Gynecology* 2005;**193**:1338–43.

Louey 2000 [pers comm] *{published data only}*
Louey K. Misoprostol for the medical management of miscarriage (ongoing trial). Personal communication 2000.

Lu 2014 *{published data only}*
Lu PH, Lu J, Zou S. Comparisons of the effects of misoprostol by two different application on the treatment of missed abortion. *Chinese Journal of Pharmaceutical Biotechnology* 2014;**21**(2):159–61.

Lughmani 2008 *{published data only}*
* Lughmani ST. A comparison of intravaginal misoprostol with prostaglandin E2 for termination of 1st trimester pregnancy. *BJOG: an international journal of obstetrics and gynaecology* 2008;**115**(s1):179.
Lughmani ST. A comparison of intravaginal misoprostol with prostaglandin E2 for termination of 1st trimester pregnancy. Double blind randomized trial [abstract]. 31st British International Congress of Obstetrics and Gynaecology; 2007 July 4-6; London, UK. 2007:209.

Machtinger 2004 *{published data only}*
Machtinger R, Stockheim D, Goldenberg M, Soriano D, Atlas M, Seidman DS. A randomized prospective study of misoprostol alone or combined with mifepristone for treatment of first trimester spontaneous abortion [abstract]. Fertility and Sterility 2002; Vol. 78, issue 3 Suppl 1:S64.
* Machtinger R, Stockheim D, Shulman A, Dulitzki M, Schiff E, Seidman DS. A randomized prospective study comparing the effectiveness of four protocols for treatment of first trimester spontaneous abortion [abstract]. *Fertility and Sterility* 2004;**82 Suppl 2**:S80.

Makhlouf 2003 *{published data only}*
Makhlouf AM, Al-Hussaini TK, Habib DM, Makarem MH. Second-trimester pregnancy termination: comparison of three different methods. *Journal of Obstetrics and Gynaecology* 2003;**23**:407–11.

Martin 1955 *{published data only}*
Martin RH, Menzies DN. Oestrogen therapy in missed abortion and labour. *Journal of Obstetrics and Gynaecology of the British Commonwealth* 1955;**62**:256–8.

Moran 2005 *{published data only}*
Moran T, Deutsch R. Methotrexate/misoprostol vs. a more standard approach for termination of pregnancies of undetermined location: a randomized, controlled trial. *Journal of Reproductive Medicine* 2005;**50**(10):784–92.

Mostafa-Gharebaghi 2010 *{published data only}*
Mostafa-Gharebaghi P, Mansourfar M, Sadeghi-Bazargani H. Low dose vaginal misoprostol versus prostaglandin E2

suppository for early uterine evacuation: a randomized clinical trial. *Pakistan Journal of Biological Sciences* 2010;**13** (19):946–50.

Muffley 2002 *{published data only}*
Muffley PE, Stitely ML, Gherman RB. Early intrauterine pregnancy failure: a randomized trial of medical versus surgical treatment. *American Journal of Obstetrics and Gynecology* 2002;**187**:321–6.

Mulayim 2009 *{published data only}*
Mulayim B, Celik NY, Onalan G, Zeyneloglu HB, Kuscu E. Sublingual misoprostol after surgical management of early termination of pregnancy. *Fertility and Sterility* 2009; **92**(2):678–81.

Nakintu 2001 *{published data only}*
Nakintu N. A comparative study of vaginal misoprostol and intravenous oxytocin for induction of labour in women with intra uterine fetal death in Mulago Hospital, Uganda. *African Health Sciences* 2001;**1**(2):55–9.

Nasreen 2009 *{published data only}*
Nasreen Z. What for early pregnancy failure manual vacuum aspiration (MVA) with small dose misoprostol or misoprostol alone?. *International Journal of Gynecology and Obstetrics* 2009;**107**(Suppl 2):S539–40.

NCT00141895 *{published data only}*
NCT00141895. A randomized trial of two regimens of misoprostol for second trimester termination for intrauterine fetal death. clinicaltrials.gov/ct2/show/ NCT00141895 (first received 1 September 2005).

NCT00190294 *{published data only}*
NCT00190294. Expectant versus immediate medical management for the evacuation of the nonevolutives pregnancies before 13 GW. clinicaltrials.gov/ct2/show/ NCT00190294 (first received 12 September 2005).

NCT00468299 *{published data only}*
NCT00468299. MiMi: a randomized trial of mifepristone and misoprostol for treatment of early pregnancy failure. clinicaltrials.gov/show/NCT00468299 (first received 1 May 2007).

Ng 2015 *{published data only}*
Ng BK, Annamalai R, Lim PS, Aqmar Suraya S, Nur Azurah AG, Muhammad Abdul Jamil MY. Outpatient versus inpatient intravaginal misoprostol for the treatment of first trimester incomplete miscarriage: a randomised controlled trial. *Archives of Gynecology and Obstetrics* 2015; **291**:105–13.

Ngai 2001 *{published data only}*
Ngai SW, Chan YM, Tang OS, Ho PC. Vaginal misoprostol as medical treatment for first trimester spontaneous miscarriage. *Human Reproduction* 2001;**16**(7):1493–6.

Ngoc 2004 *{published data only}*
Ngoc NTN, Blum J, Westheimer E, Quan TV, Winikoff B. Medical treatment of missed abortion using misoprostol. *International Journal of Gynecology and Obstetrics* 2004;**87**: 138–42.

Nielsen 1999 *{published data only}*
Nielsen S, Hahlin M, Platz-Christensen J. Expectant management or pharmacological treatment for first trimester spontaneous abortion: a randomised trial. Acta Obstetricia et Gynecologica Scandinavica 1997; Vol. 76, issue 167:77.
* Nielsen S, Hahlin M, Platz-Christensen J. Randomised trial comparing expectant with medical management for first trimester miscarriages. *British Journal of Obstetrics and Gynaecology* 1999;**106**(8):804–7.

Niromanesh 2005 *{published data only}*
Niromanesh S, Hashemi-Fesharaki M, Mosavi-Jarrahi A. Second trimester abortion using intravaginal misoprostol. *International Journal of Gynecology and Obstetrics* 2005;**89**: 276–7.

Nor Azlin 2006 *{published data only}*
Nor Azlin MI, Abdullah HS, Zainul Rashid MR, Jamil MA. Misoprostol (alone) in second trimester terminations of pregnancy: as effective as Gemeprost?. *Journal of Obstetrics and Gynaecology* 2006;**26**(6):546–9.

Nuthalapaty 2005 *{published data only}*
Nuthalapaty F, Ramsey P, Biggio J, Owen J. Comparative efficacy of high dose vaginal misoprostol for mid-trimester labor induction [abstract]. *American Journal of Obstetrics and Gynecology* 2004;**191**(6 Suppl 1):S73.
* Nuthalapaty FS, Ramsey PS, Biggio JR, Owen JO. High-dose vaginal misoprostol versus concentrated oxytocin plus low-dose vaginal misoprostol for midtrimester labor induction: a randomized trial. *American Journal of Obstetrics and Gynecology* 2005;**193**:1065–70.

Nuutila 1997 *{published data only}*
Nuutila M, Toivonen J, Ylikorkala O, Halmesmaki E. A comparison between two doses of intravaginal misoprostol and gemeprost for induction of second-trimester abortion. *Obstetrics and Gynecology* 1997;**90**(6):896–900.

Owen 1999 *{published data only}*
Owen J, Hauth JC. Vaginal misoprostol vs. concentrated oxytocin plus low-dose prostaglandin E2 for second trimester pregnancy termination. *Journal of Maternal-Fetal Medicine* 1999;**8**(2):48–50.

Pansky 2011 *{published data only}*
Pansky M, Fuchs N, Ben AI, Tovbin Y, Halperin R, Vaknin Z, et al. Intercoat (Oxiplex/AP Gel) for preventing intrauterine adhesions following operative hysteroscopy for suspected retained products of conception - A pilot study. *Journal of Minimally Invasive Gynecology* 2011;**18**(6 Suppl 1):S21.

Paraskevaides 1992 *{published data only}*
Paraskevaides E, Prendiville W, Stuart B, Scanaill SN, Walsh D, McGuinness N, et al. Medical evacuation of first trimester (twelve weeks gestation) incomplete abortion and missed abortion. *Journal of Gynecologic Surgery* 1992;**8**(3): 159–63.

Perry 1999 *{published data only}*
Perry KG, Rinehart BK, Terrone DA, Martin RW, May WL, Roberts WE. Second-trimester uterine evacuation: a comparison of intra-amniotic (15S)-15-methyl-

prostaglandin F2alpha and intravaginal misoprostol. *American Journal of Obstetrics and Gynecology* 1999;**181**: 1057–61.

Petersen 2013 ***{published data only}***

Petersen SG, Perkins A, Gibbons K, Bertolone J, Devenish-Meares P, Cave D, et al. Can we use a lower intravaginal dose of misoprostol in the medical management of miscarriage? A randomised controlled study. *Australian & New Zealand Journal of Obstetrics & Gynaecology* 2013;**53**(1):64–73.

Piotrowski 1979 ***{published data only}***

Piotrowski J, Basta A, Klimczyk K, Malolepazy A, Dluzniewska M, Splawinski JA. Indomethacin increases abortifacient effect of PGE2 in man. *Prostaglandins* 1979; **17**:451–9.

Pongsatha 2004 ***{published data only}***

Pongsatha S, Tongsong T. Intravaginal misoprostol for pregnancy termination. *International Journal of Gynecology and Obstetrics* 2004;**87**:176–7.

Ramsey 2004 ***{published data only}***

Ramsey PS, Savage K, Lincoln T, Owen J. Vaginal misoprostol versus concentrated oxytocin and vaginal PGE2 for second-trimester labor induction. *Obstetrics and Gynecology* 2004;**104**(1):138–45.

Rausch 2012 ***{published data only}***

Rausch M, Lorch S, Chung K, Frederick M, Zhang J, Barnhart K. A cost-effectiveness analysis of surgical versus medical management of early pregnancy loss. *Fertility and Sterility* 2012;**97**(2):355–60.e1.

Rita 2006 ***{published data only}***

Rita Gupta S, Kumar S. A randomised comparison of oral and vaginal misoprostol for medical management of first trimester missed abortion. *JK Science* 2006;**8**(1):35–8.

Rivero-Lopez 1998 ***{published data only}***

* Rivero-Lopez E, Marquez-Maraver F, Duenas-Diez JL, Cabezas-Sanchez B. Deferred miscarriage: effectiveness of intravaginal misoprostol versus laminaria stems [Aborto diferido: eficacia del misoprostol intravaginal versus la aplicación de tallos de laminaria]. *Progresos de Obstetricia y Ginecologia* 1998;**41**:579–81.

Roy 2003 ***{published data only}***

Roy G, Ferreira E, Hudon L, Marquette G. The efficacy of oral versus vaginal misoprostol for second-trimester termination of pregnancy: a double-blind, randomized, placebo controlled trial [abstract]. *American Journal of Obstetrics and Gynecology* 2003;**189**(6 Suppl 1):S70.

Ruangchainikhom 2006 ***{published data only}***

Ruangchainikhom W, Phongphissanou E, Bhekasuta J, Sarapak S. Effectiveness of 400 or 600 micrograms of vaginal misoprostol for terminations of early pregnancies. *Journal of the Medical Association of Thailand* 2006;**89**(7): 928–33.

Saichua 2009 ***{published data only}***

Saichua C, Phupong V. A randomized controlled trial comparing powdery sublingual misoprostol and sublingual misoprostol tablet for management of embryonic death or anembryonic pregnancy. *Archives of Gynecology and Obstetrics* 2009;**280**(3):431–5.

Salamalekis 1990 ***{published data only}***

Salamalekis E, Loghis C, Kassanos D, Traka A, Zourlas PA. Comparison of extra-amniotic prostaglandin F2alpha and dinoprostone use for labor induction after second trimester intrauterine fetal death. 12th European Congress of Perinatal Medicine; 1990 Sept 11-14; Lyon, France. 1990:228.

Sathapanachai 2000 ***{published data only}***

Sathapanachai U. Intravaginal 400 micrograms misoprostol for pregnancy termination in cases of blighted ovum. *Thai Journal of Obstetrics and Gynaecology* 2000;**12**(4):363.

Shah 2010 ***{published data only}***

Shah N, Azam SI, Khan NH. Sublingual versus vaginal misoprostol in the management of missed miscarriage. *JPMA - Journal of the Pakistan Medical Association* 2010;**60** (2):113–6.

Shaikh 2008 ***{published data only}***

Shaikh ZAN. Comparison between misoprostol alone and misoprostol with manual vacuum aspiration for the treatment of missed and incomplete miscarriage. *BJOG: an international journal of obstetrics and gynaecology* 2008;**115** (s1):83.

Shobeira 2007 ***{published data only}***

Shobeira JM, Atashkhoii S. Second trimester pregnancy termination by intravaginal and parenteral form of prostaglandin E2 [abstract]. 31st British International Congress of Obstetrics and Gynaecology; 2007 July 4-6; London, UK. 2007:210.

Shokry 2009 ***{published data only}***

Shokry M, Shahin AY, Fathalla MM, Shaaban OM. Oral misoprostol reduces vaginal bleeding following surgical evacuation for first trimester spontaneous abortion. *International Journal of Gynecology and Obstetrics* 2009;**107** (2):117–20.

Shuaib 2013 ***{published data only}***

Shuaib AA, Alharazi AH. Medical versus surgical termination of the first trimester missed miscarriage. *Alexandria Journal of Medicine* 2013;**49**:13–6.

Sonsanoh 2014 ***{published data only}***

Sonsanoh A, Chullapram T. Comparison of sublingual and vaginal misoprostol for termination of early pregnancy failure: a randomized controlled trial. *Thai Journal of Obstetrics and Gynaecology* 2014;**22**(3):128–36.

Sripramote 2000 ***{published data only}***

Sripramote M, Chatsuphang W. A randomized comparison of oral and vaginal misoprostol for cervical priming before uterine curettage in the first trimester of pregnancy. *Vajira Medical Journal* 2000;**44**(3):207–15.

Stockheim 2006 ***{published data only}***

Stockheim D, Machtinger R, Wiser A, Dulitzky M, Soriano D, Goldenberg M, et al. A randomized prospective study of misoprostol or mifepristone followed by misoprostol when needed for the treatment of women with early pregnancy failure. Fertility and Sterility 2006; Vol. 86, issue 4:956–60.

Su 2005 *{published data only}*
Su L-L, Biswas A, Choolani M, Kalaichelvan V, Singh K. A prospective, randomized comparison of vaginal misoprostol versus intra-amniotic prostaglandins for midtrimester termination of pregnancy. *American Journal of Obstetrics and Gynecology* 2005;**193**:1410–4.

Suchonwanit 1999 *{published data only}*
Suchonwanit P. Comparative study between vaginal misoprostol 200 mg and 400 mg in first trimester intrauterine fetal death and anembryonic gestation. *Thai Journal of Obstetrics and Gynaecology* 1999;**11**(4):263.

Surita 1997 *{published data only}*
Surita FGC. Misoprostol versus laminaria for cervical ripening in intrauterine fetal death. *Acta Obstetricia et Gynecologica Scandinavica Supplement* 1997;**76**(167):32.

Tang 2003 *{published data only}*
Tang OS, Lau WNT, Ng EHY, Lee SWH, Ho PCH. A prospective randomized study to compare the use of repeated doses of vaginal with sublingual misoprostol in the management of first trimester silent miscarriage. *Human Reproduction* 2003;**18**(1):176–81.

Tang 2006a *{published data only}*
Tang OS, Ong CY, Tse KY, Ng EH, Lee SW, Ho PC. A randomized trial to compare the use of sublingual misoprostol with or without an additional 1 week course for the management of first trimester silent miscarriage. *Human Reproduction* 2006;**21**(1):189–92.

Tanha 2010 *{published data only}*
Tanha FD. Comparison of the efficacy of two routes of misoprostol administration (sublingual and vaginal) for termination of second trimester pregnancy. en.search.irct.ir/view/1614 Date first received: 28 November 2010.
* Tanha FD, Feizi M, Shariat M. Sublingual versus vaginal misoprostol for the management of missed abortion. *Journal of Obstetrics and Gynaecology Research* 2010;**36**(3):525–32.

Thavarasah 1986 *{published data only}*
Thavarasah AS, Almohdzar SA. Prostaglandin (F2 alpha) in missed abortion Intravenous, extra-amniotic and intramuscular administration--a randomized study. *Biological Research in Pregnancy and Perinatology* 1986;**7**:106–10.

Thida 2015 *{published data only}*
Thida M, Shwe MM, Htun KT, Maung NM, Khine EP, Win KSM, et al. A randomised clinical trial comparing different routes of administration of repeated doses of 400ug misoprostol for management of missed miscarriages and anembryonic gestations in North Okkalapa General Hospital, Yangon, Myanmar. *BJOG: an international journal of obstetrics and gynaecology* 2015;**122**(Suppl S1):26–7.

Toppozada 1994 *{published data only}*
Toppozada MK, Shaala SA, Anwar MY, Haiba NA, Abdrabbo S, El-Absy HM. Termination of pregnancy with fetal death in the second and third trimesters - the double balloon versus extra-amniotic prostaglandin. *International Journal of Gynecology and Obstetrics* 1994;**45**:269–73.

Torre 2012 *{published data only}*
Torre A, Huchon C, Bussieres L, Machevin E, Camus E, Fauconnier A. Immediate versus delayed medical treatment for first-trimester miscarriage: a randomized trial. *American Journal of Obstetrics and Gynecology* 2012;**206**(3):215.e1–6.

Wood 2002 *{published data only}*
Wood SL, Brain PH. Medical management of missed abortion: a randomized clinical trial. *Obstetrics and Gynecology* 2002;**99**(4):563–6.

Yapar 1996 *{published data only}*
Yapar EG, Senoz S, Urkutur M, Batioglu S, Gokmen O. Second trimester pregnancy termination including fetal death: comparison of five different methods. *European Journal of Obstetrics, Gynecology, and Reproductive Biology* 1996;**69**:97–102.

Yilmaz 2005 *{published data only}*
Yilmaz B, Kelekci S, Ertas IE, Kahyaoglu S, Ozel M, Sut N, et al. Misoprostol moistened with acetic acid or saline for second trimester pregnancy termination: a randomized prospective double-blind trial. *Human Reproduction* 2005;**20**(11):3067–71.

Yilmaz 2007 *{published data only}*
Yilmaz B, Kelekci S, Ertas IE, Ozel M, Sut N, Mollamahmutoglu L, et al. Randomized comparison of second trimester pregnancy termination utilizing saline moistened or dry misoprostol. *Archives of Gynecology and Obstetrics* 2007;**276**(5):511–6.

Yu 2000 *{published data only}*
Yu X H. Clinical observation of 42 cases of mifepristone and Misoprostol in missed abortion. *Journal of Chinese Medical Writing* 2000;**7**(5):552–3.

Zhang 2000 *{published data only}*
Zhang C, Cheng W. A contrastive analysis of the efficacy of misoprostol and li fan nuo in intermediate term of pregnancy. *Journal of Wuhan University of Science and Technology (Natural Science Edition)* 2000;**23**(4):409–11.

References to ongoing studies

ISRCTN65305620 *{published data only}*
ISRCTN65305620. Is misoprostol a safe alternative to manual vacuum aspiration in women with early pregnancy failure in a low resource setting?. www.isrctn.com/ISRCTN65305620 (first received 1 February 2008).

NCT01033903 *{published data only}*
NCT01033903. Which is the optimal treatment for miscarriage with a gestational sac in the uterus and which factors can predict if the treatment will be successful? [Optimal treatment of miscarriage]. clinicaltrials.gov/show/NCT01033903 (first received 16 December 2009).

Additional references

Aleman 2005
Aleman A, Althabe F, Belizán J, Bergel E. Bed rest during pregnancy for preventing miscarriage. *Cochrane Database of Systematic Reviews* 2005, Issue 2. [DOI: 10.1002/14651858.CD003576.pub2]

Alfirevic 2014
Alfirevic Z, Alfaifel N, Weeks A. Oral misoprostol for induction of labour. *Cochrane Database of Systematic Reviews* 2014, Issue 6. [DOI: 10.1002/14651858.CD001338.pub3]

Ankum 2001
Ankum WM, Wieringa-de Waard M, Bindels PJE. Management of spontaneous miscarriage in the first trimester: an example of putting informed shared decision making into practice. *BMJ* 2001;**322**:1343–6.

Arthur 2007
Arthur P, Taggart MJ, Mitchell BF. Oxytocin and parturition: a role for increased myometrial calcium and calcium sensitization?. *Frontiers in Bioscience* 2007;**12**:619–33.

Atkins 2004
Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, et al. GRADE Working Group. Grading quality of evidence and strength of recommendations. *BMJ* 2008;**328**(7454):1490.

Balogun 2016
Balogun O, da Silva Lopes K, Ota E, Takemoto Y, Rumbold A, Takegata M, et al. Vitamin supplementation for preventing miscarriage. *Cochrane Database of Systematic Reviews* 2016, Issue 5. [DOI: 10.1002/14651858.CD004073.pub4]

Bamigboye 2003
Bamigboye AA, Morris J. Oestrogen supplementation, mainly diethylstilbestrol, for preventing miscarriages and other adverse pregnancy outcomes. *Cochrane Database of Systematic Reviews* 2003, Issue 3. [DOI: 10.1002/14651858.CD004353]

Calvache 2012
Calvache JA, Delgado-Noguera MF, Lesaffre E, Stolker RJ. Anaesthesia for evacuation of incomplete miscarriage. *Cochrane Database of Systematic Reviews* 2012, Issue 4. [DOI: 10.1002/14651858.CD008681.pub2]

Chung 1995
Chung TKH, Cheung LP, Leung TY, Haines CJ, Chang AMZ. Misoprostol in the management of spontaneous abortion. *British Journal of Obstetrics and Gynaecology* 1995;**102**:832–5.

Costa 1993
Costa SH, Vessey MP. Misoprostol and illegal abortion in Rio de Janeiro, Brazil. *Lancet* 1993;**341**:1258–61.

de Jong PG 2014
de Jong PG, Kaandorp S, Di Nisio M, Goddijn M, Middeldorp S. Aspirin and/or heparin for women with unexplained recurrent miscarriage with or without inherited thrombophilia. *Cochrane Database of Systematic Reviews* 2014, Issue 7. [DOI: 10.1002/14651858.CD004734.pub4]

Dodd 2010
Dodd JM, Crowther CA. Misoprostol for induction of labour to terminate pregnancy in the second or third trimester for women with a fetal anomaly or after intrauterine fetal death. *Cochrane Database of Systematic Reviews* 2010, Issue 4. [DOI: 10.1002/14651858.CD004901]

Empson 2005
Empson M, Lassere M, Craig J, Scott J. Prevention of recurrent miscarriage for women with antiphospholipid antibody or lupus anticoagulant. *Cochrane Database of Systematic Reviews* 2005, Issue 2. [DOI: 10.1002/14651858.CD002859.pub2]

Fonseca 1991
Fonseca W, Alencar AJC, Mota FSB, Coelho HLL. Misoprostol and congenital malformations. *Lancet* 1991;**338**:56.

Haas 2013
Haas DM, Ramsey PS. Progestogen for preventing miscarriage. *Cochrane Database of Systematic Reviews* 2013, Issue 10. [DOI: 10.1002/14651858.CD003511.pub3]

Harris 2007
Harris LH, Dalton VK, Johnson TRB. Surgical management of early pregnancy failure: history, politics, and safe, cost-effective care. *American Journal of Obstetrics and Gynecology* 2007;**196**(5):445.e1–5.

Harwood 2008
Harwood B, Nansel T, the National Institute of Child Health and Human Development Management of Early Pregnancy Failure Trial. Quality of life and acceptability of medical versus surgical management of early pregnancy failure. *BJOG: an international journal of obstetrics and gynaecology* 2008;**115**(4):501–8.

Hawk 1985
Hawk HW, Conley HH. Effect of prostaglandin F2 alpha, phenylephrine and ergonovine on uterine contractions in the ewe. *Journal of Animal Science* 1985;**60**(2):537–43.

Higgins 2011
Higgins JP, Green S, editor(s). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from handbook.cochrane.org.

Hofmeyr 2010
Hofmeyr GJ, Gülmezoglu AM, Pileggi C. Vaginal misoprostol for cervical ripening and induction of labour. *Cochrane Database of Systematic Reviews* 2010, Issue 10. [DOI: 10.1002/14651858.CD000941]

Jain 2002
Jain JK, Dutton C, Harwood B, Meckstroth KR, Mishell DR Jr. A prospective randomized, double-blinded, placebo-controlled trial comparing mifepristone and vaginal misoprostol to vaginal misoprostol alone for elective termination of early pregnancy. *Human Reproduction* 2002;**17**(6):1477–82.

Kawarabayashi 1990
Kawarabayashi T, Kishikawa T, Sugimori H. Effect of methylergometrine maleate (methergin) on electrical and mechanical activities of pregnant human myometrium. *Gynecologic and Obstetric Investigation* 1990;**24**(4):246–9.

Klier 2002
Klier CM, Geller PA, Ritsher JB. Affective disorders in the aftermath of miscarriage: a comprehensive review. *Archives of Women's Mental Health* 2002;**5**:129–49.

Kulier 2011
Kulier R, Kapp N, Gülmezoglu AM, Hofmeyr GJ, Cheng LN, Campana A. Medical methods for first trimester abortion. *Cochrane Database of Systematic Reviews* 2011, Issue 11. [DOI: 10.1002/14651858.CD002855.pub3]

Lewis 2007
Lewis G, editor. *The Confidential Enquiry into Maternal and Child Health (CEMACH). Saving mothers' lives: reviewing maternal deaths to make motherhood safer - 2003-2005. The seventh report on confidential enquiries into maternal deaths in the United Kingdom*. London: CEMACH, 2007.

Lohr 2008
Lohr PA, Hayes JL, Gemzell-Danielsson K. Surgical versus medical methods for second trimester induced abortion. *Cochrane Database of Systematic Reviews* 2008, Issue 1. [DOI: 10.1002/14651858.CD006714.pub2]

Lok 2007
Lok IH, Neugebauer R. Psychological morbidity following miscarriage. *Best Practice & Research. Clinical Obstetrics & Gynaecology* 2007;**21**(2):229–47.

Luise 2002
Luise C, Jermy K, May C, Costello G, Collins WP, Bourne TH. Outcome of expectant management of spontaneous first trimester miscarriage: observational study. *BMJ* 2002; **324**:873–5.

Mota-Rojas 2007
Mota-Rojas D, Villanueva-García D, Velazquez-Armenta EY, Nava-Ocampo AA, Ramírez-Necoechea R, Alonso-Spilsbury M, et al. Influence of time at which oxytocin is administered during labor on uterine activity and perinatal death in pigs. *Biological Research* 2007;**40**(1):55–63.

Murphy 2012
Murphy FA, Lipp A, Powles DL. Follow-up for improving psychological well being for women after a miscarriage. *Cochrane Database of Systematic Reviews* 2012, Issue 3. [DOI: 10.1002/14651858.CD008679.pub2]

Nanda 2012
Nanda K, Lopez LM, Grimes DA, Peloggia A, Nanda G. Expectant care versus surgical treatment for miscarriage. *Cochrane Database of Systematic Reviews* 2012, Issue 3. [DOI: 10.1002/14651858.CD003518.pub3]

Neilson 2006
Neilson JP, Hickey M, Vazquez J. Medical treatment for early fetal death (less than 24 weeks). *Cochrane Database of Systematic Reviews* 2006, Issue 3. [DOI: 10.1002/14651858.CD002253.pub3]

Norman 1991
Norman JE, Thong KJ, Baird DT. Uterine contractility and induction of abortion in early pregnancy by misoprostol and mifepristone. *Lancet* 1991;**338**:1233–6.

Ramphal 2006
Ramphal SR, Moodley J. Emergency gynaecology. *Best Practice & Research. Clinical Obstetrics & Gynaecology* 2006; **20**(5):729–50.

RCOG 2006
Royal College of Obstetricians and Gynaecologists. *The Management of Early Pregnancy Loss. Royal College of Obstetricians and Gynaecologists, Guideline No. 25*. London: RCOG, 2006.

RevMan 2014 [Computer program]
Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager 5 (RevMan 5). Version 5.3. Copenhagen: Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

Sawyer 2007
Sawyer E, Ofuasia E, Ofili-Yebovi D, Helmy S, Gonzalez J, Jurkovic D. The value of measuring endometrial thickness and volume on transvaginal ultrasound scan for the diagnosis of incomplete miscarriage. *Ultrasound in Obstetrics & Gynecology* 2007;**29**(2):205–9.

Say 2010
Say L, Brahmi D, Kulier R, Campana A, Gülmezoglu M. Medical versus surgical methods for first trimester termination of pregnancy. *Cochrane Database of Systematic Reviews* 2010, Issue 3. [DOI: 10.1002/14651858.CD003037.pub2]

Shiers 2003
Shiers C. Abnormalities of early pregnancy. In: Fraser DM, Cooper MA editor(s). *Myles Textbook for Midwives*. 14th Edition. Edinburgh: Churchill Livingstone, 2003.

Smith 2009
Smith LFP, Ewings PD, Quinlan C. Incidence of pregnancy after expectant, medical, or surgical management of spontaneous first trimester miscarriage: long term follow-up of miscarriage treatment (MIST) randomised controlled trial. *BMJ* 2009;**339**(1766):b3827.

Swanson 1999
Swanson KM. Effects of caring, measurement, and time on miscarriage impact and women's well-being. *Nursing Research* 1999;**48**(6):288–98.

Tang 2006b
Tang OS, Ho PC. The use of misoprostol for early pregnancy failure. *Current Opinion in Obstetrics and Gynecology* 2006;**18**(6):581–6.

Thapar 1992
Thapar AK, Thapar A. Psychological sequelae of miscarriage: a controlled study using the general health questionnaire and the hospital anxiety and depression scale. *British Journal of General Practice* 1992;**42**(356):94–6.

Tuncalp 2010
Tuncalp O, Gülmezoglu AM, Souza JP. Surgical procedures for evacuating incomplete miscarriage. *Cochrane Database of Systematic Reviews* 2010, Issue 9. [DOI: 10.1002/14651858.CD001993.pub2]

Tuncalp 2012
Tunçalp Ö, Hofmeyr GJ, Gülmezoglu AM. Prostaglandins for preventing postpartum haemorrhage. *Cochrane Database of Systematic Reviews* 2012, Issue 8. [DOI: 10.1002/14651858.CD000494.pub4]

Weeks 2001
Weeks A, Alia G. Ultrasonography may have role in assessing spontaneous miscarriage. *BMJ* 2001;**323**:694.

Wildschut 2011
Wildschut HIJ, Both MI, Medema S, Thomee E, Wildhagen MF, Kapp N. Medical methods for mid-trimester termination of pregnancy. *Cochrane Database of Systematic Reviews* 2011, Issue 1. [DOI: 10.1002/14651858.CD005216.pub2]

Wong 2014
Wong LF, Porter TF, Scott JR. Immunotherapy for recurrent miscarriage. *Cochrane Database of Systematic Reviews* 2014, Issue 10. [DOI: 10.1002/14651858.CD000112.pub3]

Zieman 1997
Zieman M, Fong SK, Benowitz NL, Bankster D, Darney PD. Absorption kinetics of misoprostol with oral or vaginal administration. *Obstetrics and Gynecology* 1997;**90**:88–92.

References to other published versions of this review

Neilson 2008
Neilson JP, Gyte GML, Hickey M, Vazquez JC. Medical treatments for incomplete miscarriage (less than 24 weeks). *Cochrane Database of Systematic Reviews* 2008, Issue 3. [DOI: 10.1002/14651858.CD007223]

Neilson 2010
Neilson JP, Gyte GML, Hickey M, Vazquez JC, Dou L. Medical treatments for incomplete miscarriage (less than 24 weeks). *Cochrane Database of Systematic Reviews* 2010, Issue 1. [DOI: 10.1002/14651858.CD007223.pub2]

Neilson 2013
Neilson JP, Gyte GML, Hickey M, Vazquez JC, Dou L. Medical treatments for incomplete miscarriage. *Cochrane Database of Systematic Reviews* 2013, Issue 3. [DOI: 10.1002/14651858.CD007223.pub3]

* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Bique 2007

Methods	RCT with randomisation of individual women. Using computer-generated random numbers in sequentially numbered opaque envelopes
Participants	Inclusion criteria • Women with confirmed incomplete spontaneous or induced miscarriage, less than 12 weeks' gestation • Diagnosis was based on past or present history of vaginal bleeding during pregnancy and an open cervical os • > 18 years; no known allergy to misoprostol; no signs of severe infection; no haemodynamic disturbance; lived or worked within the hospitals geographic area of coverage • N = 270 women but 23 lost due to a problem with randomisation, leaving 247 women Exclusion criteria • Nothing specified other than inclusion criteria
Interventions	Intervention: oral misoprostol • 600 ug single-dose • N = 123 Comparison: surgery • MVA • N = 124
Outcomes	Complete miscarriage without recourse to additional surgical intervention, experience of side effects and acceptability of treatment • Appears to be clinical assessment of complete miscarriage • Women were assessed at 1 week • If miscarriage was still incomplete, women were given the option to wait another week or have surgery then • Women who chose to wait were reassessed 1 week later and if still no complete miscarriage, then surgery
Notes	1. Setting: tertiary hospital in Mozambique. 2. If miscarriage incomplete at 7 days, women were given the option to wait another week or have surgery then. Women who chose to wait and were still incomplete at 2 weeks were then given surgery. 3. Additional outcomes assessed but not prespecified in the review: bleeding; pain/cramps; fever; chills; tolerability; would choose method again; would recommend method to a friend; best and worst features.

Risk of bias			*Risk of bias*
Bias	**Authors' judgement**	**Support for judgement**	

Bique 2007 (*Continued*)

Random sequence generation (selection bias)	Low risk	"The randomisation scheme was generated by computer..."
Allocation concealment (selection bias)	Low risk	"...treatment allocations printed on cards inserted into sequentially numbered opaque envelopes...a member of the study staff opened the next envelope in the sequence and assigned to women to the indicated treatment group."
Blinding of participants and personnel (performance bias) All outcomes	High risk	It was not possible to blind people and this is discussed by authors
Blinding of outcome assessment (detection bias) All outcomes	High risk	It was not possible to blind people and this is discussed by authors
Incomplete outcome data (attrition bias) All outcomes	Low risk	• 23 women were excluded after randomisation because of a problem identified with the randomisation process as discussed by authors. • 35 women did not return at 1 week: 12 from misoprostol group and 23 from MVA group. • 10 women in misoprostol group had MVA prior to the 1 week follow-up time. These were included in the misoprostol group. • Not strictly speaking ITT analysis, but outcomes on the 23 women excluded were reported and similar to those included. Analysis was done on 212 women on whom data were available.
Selective reporting (reporting bias)	Unclear risk	As far as can tell, outcomes reported were those prespecified, however the trial protocol was not assessed
Other bias	Unclear risk	The 2 groups were comparable on background characteristics. But the paper mentioned that "in the process of monitoring the first 20 cases, it was noted that the randomisation scheme was not being appropriately followed - the study was restarted". More women were lost to follow-up in the MVA group than the misoprostol group

Blanchard 2004

Methods	RCT with randomisation of individual women. Sequentially numbered opaque envelopes, using pseudo-random number generator
Participants	Inclusion criteria • Women with signs of incomplete miscarriage • Diagnosis confirmed by ultrasound • 1st trimester; good general health; no allergy to misoprostol; good access to emergency facilities • N = 169 women Exclusion criteria • None specified
Interventions	Intervention: oral misoprostol • 600 ug, single-dose • N = 86 Comparison: oral misoprostol • 1200 ug, 2 doses, 4 hours apart • N = 83
Outcomes	Complete miscarriage at 48 hours; surgical evacuation; side effects and acceptability • Assessed by ultrasound at 48 hours • If miscarriage not complete at 48 hours, women were given the option to wait additional 5 days (1 week from misoprostol administration) to see if miscarriage would be complete without further intervention. If miscarriage not complete after 1 week or if woman refused extension, then she underwent surgical evacuation according to standard practice
Notes	1. Setting: 2 teaching hospitals in Bangkok, Thailand. 2. Additional outcomes assessed but not prespecified in the review: bleeding (heavy, normal, spotting); pain; fever; medically necessary interventions; satisfied or very satisfied with treatment.

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"Pseudo-random number generator in SSPS 9.0."
Allocation concealment (selection bias)	Low risk	Women given the next "...sequentially numbered opaque envelope; the number in the envelope became her study identification number"
Blinding of participants and personnel (performance bias) All outcomes	High risk	"Neither the provider nor the woman was blinded to the treatment regimes."

Blanchard 2004 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	High risk	"Neither the provider nor the woman was blinded to the treatment regimes."
Incomplete outcome data (attrition bias) All outcomes	Low risk	2 women in single-dose group and 1 woman in double-dose group were lost to follow-up. 1.8% of total, so no real impact.
Selective reporting (reporting bias)	Unclear risk	Appears to be free of selective reporting bias but we did not assess the trial protocol
Other bias	Low risk	Appears to be free of other reporting bias.

Blohm 2005

Methods	RCT with randomisation of individual women.
Participants	Inclusion criteria • Women seeking medical attention due to signs of miscarriage in 1st trimester • To be included, women had to be circulatory stable (stable blood pressure and Hb > 90 g/L) and without any signs of genital infection. Only women with a gestational residue (A-P diameter) between 15 mm and 50 mm were included. The non-viability of the concepts had to be confirmed and accepted by both the physician and woman. Only women above the age of 18 were included • Vaginal ultrasound confirmed the miscarriage diagnosis • N = 126 women Exclusion criteria • Women who were not able to understand the information provided regarding the study and women with a possible allergy or medical contraindication for analgesics or misoprostol were not included
Interventions	Intervention: vaginal misoprostol • 400 ug; 2 tablets of 200 ug, each self-administered at home • N = 64 Comparison: placebo • tablets identical with the misoprostol tablets • N = 62
Outcomes	Complete miscarriage assessed at 6-7 days; infection; bleeding; gastrointestinal side effects; subjective pain; use of analgesics and length of sick leave • Assessed at 7 days • Successful miscarriage was defined as A-P diameter for the gestational residue was < 15 mm
Notes	1. Setting: University Hospital, Goteborg, Sweden 2. Confirmed with the author that the women had incomplete miscarriages diagnosed by ultrasound and there were no IUFDs

Blohm 2005 (*Continued*)

	3. Additional outcomes assessed but not prespecified in the review: serum Hb; reduction in serum Hb and days of sick leave

Risk of bias ***Risk of bias***

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"...random table system..."
Allocation concealment (selection bias)	Low risk	"Patients were randomised...by drawing a sealed envelope from a box...tablets were delivered to the independent pharmacy where they were inserted by the pharmacy staff into numbered envelopes in blocks of 10...the randomisation list was retained by the hospital pharmacy and was not broken until after completion of the study when statistical analyses were performed." However, no mention of the envelopes being opaque - so concealment allocation unclear but because tablets are identical, it seems unlikely there is a problem here
Blinding of participants and personnel (performance bias) All outcomes	Low risk	The placebo tablets "...were identical in appearance to the active misoprostol tablets" and clinicians "...unaware of the randomisation sequence."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The placebo tablets "...were identical in appearance to the active misoprostol tablets" and clinicians "...unaware of the randomisation sequence."
Incomplete outcome data (attrition bias) All outcomes	Low risk	There was no loss to follow-up and women received their appropriate allocation. The analysis appears to be ITT
Selective reporting (reporting bias)	Unclear risk	Seems to be free of bias here, although the secondary outcome of 'total number of days of bleeding' was not reported. However, we did not assess the trial protocol
Other bias	Unclear risk	1. There was an imbalance in baseline data for gestational age: misoprostol: 72.8 (SD 12.2) and placebo 77.8 (SD 12.9). This might favour better outcomes for the placebo group, but probably no important bias here.

Blohm 2005 (*Continued*)

		2. Women chose whether they wanted a D&C if miscarriage not complete after 1 week or whether to wait longer. So we used the outcome of complete miscarriage at 1 week which excludes problems with choice after that time, but the problem is present for the outcome of surgical evacuation.

Chigbu 2012

Methods	Open-label RCT with randomisation of individual women.
Participants	Inclusion criteria • Open cervical os, vaginal bleeding or history of vaginal bleeding during this pregnancy • Uterine size less than or equal to 12 weeks' LMP • Willingness to return for follow-up in 1 week • No known contraindications to misoprostol • General good health Exclusion criteria • Signs of severe infection (foul-smelling discharge, fever > 38 degrees Celsius, pulse > 110/minute) • Known allergy to misoprostol or other prostaglandin • Suspected ectopic pregnancy • Haemodynamic instability or shock
Interventions	Intervention: oral misoprostol • Misoprostol 600 mcg orally • N = 160 Control: surgical evacuation • MVA • N = 160
Outcomes	Primary outcome measure: complete uterine evacuation after initial treatment • Assessed at 1 week follow-up visit with bimanual exam and speculum • If still incomplete, woman was given choice to wait one more week without any further intervention or immediate surgical evacuation • If at the 2nd follow-up visit, woman was still incomplete, underwent MVA Other outcome measures included adverse effects from the treatment and satisfaction/ acceptability • Assessed by observation and by exit interview • Pain intensity measured by 7-point Likert scale • Satisfaction measured by 5-point Likert scale
Notes	Setting: a small private clinic with a large rural catchment area in a resource-poor country in sub-Saharan Africa - South-Eastern Nigeria. Ekeakpara, a rural community in Osi-sioma Ngwa Local Government Area of Abia State, Nigeria All participants, regardless of assigned treatment were given prophylactic antibiotics, and

Chigbu 2012 (*Continued*)

	paracetamol tablets to help manage their pain. They were observed in the clinic for a maximum of 3 hours after treatment and, in absence of danger signs, discharged Women allocated to MVA (Ipas, Chapel Hill, NC, USA) were given surgical evacuation by a trained doctor in the MVA room at the clinic using reassurance alone and no anaesthesia during the procedure

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Sequentially numbered envelopes. When a new participant was enrolled in the study, a trained nurse would open the next envelope in the numbered series and the woman would receive the treatment specified therein. No mention of random number table or using a computer random number generator to order envelopes
Allocation concealment (selection bias)	Unclear risk	Sealed envelopes - no mention of opaque envelopes.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open-label; no blinding.
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding performed.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No attrition.
Selective reporting (reporting bias)	Unclear risk	Trial protocol not published.
Other bias	Low risk	We did not identify any other biases.

Clevin 2001

Methods	RCT with randomisation of individual women.
Participants	Inclusion criteria • Women with miscarriage up to 12 weeks' gestation • Transvaginal ultrasound used • Only those women (N = 34) with endometrial thickness > 10 cm were randomised, the remaining women (N = 27) had endometrial thickness < 10 cm an were managed by expectancy • N = 61 women

Clevin 2001 (*Continued*)

	Exclusion criteria • Women with intrauterine device in situ, missed abortion flow/blighted ovum, extrauterine pregnancy or molar
Interventions	Intervention: vaginal prostaglandin • Prostaglandin E1 analogue (gemeprost) • N = 17 Comparison 1: surgical management • Curettage • N = 17 Comparison 2: expectant management • Women were not randomised to this group but selected on clinical grounds
Outcomes	Duration of vaginal bleeding; pain; discomfort experienced; sick days and days of absence • Assessed at 5-8 days using transvaginal ultrasound
Notes	1. Setting: district hospital in Glostrup, Copenhagen, Denmark. 2. Paper written in Danish, with English abstract. Paper was translated. 3. Additional outcomes assessed but not prespecified in the review: bleeding; pain; days of sick leave; women's dissatisfaction. The participants were divided into 2 groups: • Group 1 (27) with an endometrial thickness of less than 10 mm; and • Group 2 (34) with an endometrial thickness greater than 10 mm Group 1 was managed by expectancy and Group 2 was further divided into 2 groups again at random: • Group 2 A (17) which was given Prostaglandin E1 analogue gemeprost (1 mg) • Group 2 B (17) which underwent curettage This review looked only at group 2A versus 2B.

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"The participating women were chosen at random by the drawing of lots into 2 parallel groups."
Allocation concealment (selection bias)	Unclear risk	"The participating women were chosen at random by the drawing of lots into 2 parallel groups." No further information
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible to blind women nor clinicians.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No mention of whether assessors were blinded or not.

Clevin 2001 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	4 women did not complete the trial period. 2 from gemeprost group and 0 from curettage group (2 from expectant group). 6% loss but both from the medical management group
Selective reporting (reporting bias)	Unclear risk	There is no mention of the outcomes to be measured although there was a questionnaire sent to women and this may well have been designed before the study began. Also, we did not assess the trial protocol
Other bias	Low risk	"The patients in all groups were comparable regarding age, previous births and previous spontaneous or instigated abortions. " There was no other information which would suggest other biases

Dabash 2010

Methods	Randomised trial.
Participants	Inclusion criteria • women with clinical diagnosis of incomplete miscarriage (open cervix, vaginal bleeding, ultrasound confirmation in around a third of cases) • attending two large tertiary maternity units in Egypt: in Cairo and Alexandria • N = 697
Interventions	Intervention: misoprostol • 400 mcg sublingually • N = 349 but one lost to follow-up, leaving 348 Comparison: surgery • MVA • N = 348 but one lost to follow-up, leaving 347
Outcomes	Primary: completed miscarriage. Secondary: additional evacuation of uterus; drop in Hb by > 2 g/dL; satisfaction; adverse effects
Notes	Trial performed 2007-2008.

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated random number allocation in batches of 10

Dabash 2010 (*Continued*)

Allocation concealment (selection bias)	Low risk	Sequentially numbered envelopes.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No attempt at blinding.
Blinding of outcome assessment (detection bias) All outcomes	High risk	No attempt at blinding.
Incomplete outcome data (attrition bias) All outcomes	Low risk	2/697 women lost to follow-up.
Selective reporting (reporting bias)	Unclear risk	We did not assess the trial protocol.
Other bias	Low risk	No other apparent biases.

Dao 2007

Methods	RCT with randomisation of individual women, in blocks of 10 and stratified by site (2 sites involved)
Participants	Inclusion criteria • Women with incomplete spontaneous or induced miscarriage, less than 12 weeks' gestation, diagnosed using ultrasound • Uterine size equivalent to a gestation of less than 12 weeks LMP, open cervical os, past or present history of vaginal bleeding during pregnancy and ultrasound evidence of substantial uterine debris with evidence of fetal demise • Women living or working within the hospital's geographical area of coverage, no known contraindications to misoprostol, no signs of severe infection, temperature < 38 ^{o}C and general good health • N = 460 women Exclusion criteria • Women with very high fever; signs of severe infection
Interventions	Intervention: oral misoprostol • 600 ug, single-dose • N = 233 Comparison: surgery • MVA • N = 227
Outcomes	Complete miscarriage following initial treatment; adverse effects, bleeding; pain (7-point Likert scale), acceptability (5-point Likert scale) • Assessed at 1 week using clinical assessments and US. Women could wait a further week before surgery (MVA) if they wished

Dao 2007 (*Continued*)

Notes	1. Setting: 2 large university teaching hospitals in Burkina Faso, sub-Saharan Africa. 2. Additional outcomes assessed but not prespecified in the review: pain/cramps; fever; chills; bleeding; overall experience; overall satisfaction; would choose again; would recommend to a friend; hospitalisation; managed pain with paracetamol; would have liked stronger pain killers; sought contact with providers; made phone calls to providers; best and worst features.

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"...computer-generated random sequence provided by Genunity Health Projects..."
Allocation concealment (selection bias)	Low risk	"The assignment was concealed from providers and participants until after informed consent was given when the next sequential opaque sealed study envelope was opened to reveal allocation..."
Blinding of participants and personnel (performance bias) All outcomes	High risk	"Neither women nor providers were blinded to treatment assignment..."
Blinding of outcome assessment (detection bias) All outcomes	High risk	"Neither women nor providers were blinded to treatment assignment..."
Incomplete outcome data (attrition bias) All outcomes	Low risk	• Lost after randomisation and before prescription: 10 in misoprostol group and 3 in the MVA group • Exclusion after randomisation: 5 in the misoprostol group and 1 in the MVA group • Overall, there were uneven loses to follow-up and some exclusions, but as numbers are small, we think this is unlikely to cause bias
Selective reporting (reporting bias)	Unclear risk	Prespecified outcomes reported on, but the trial protocol not assessed
Other bias	Low risk	No apparent biases from other sources. Baseline data showed no statistically significant differences between the groups

Diop 2009

Methods	RCT with randomisation of individual women. Non-equivalence trial
Participants	Inclusion criteria • Women with incomplete miscarriage with uterine size < 12 weeks' gestation based on clinical diagnosis (mainly open cervix, vaginal bleeding) • Ultrasound sometimes used to confirm diagnosis • N = 300 but 6 lost to follow-up, leaving 294
Interventions	Intervention: sublingual misoprostol • 400 mcg • N = 150 but 4 lost to follow-up, leaving 146 Comparison: oral misoprostol • 600 mcg • N = 150 but 2 lost to follow-up, leaving 148
Outcomes	Complete miscarriage, satisfaction, side effects and pain.
Notes	Two settings: large tertiary maternity hospitals in Madagascar (n = 200) and Moldova (n = 100)

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated random number allocation.
Allocation concealment (selection bias)	Low risk	Sealed opaque envelopes.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No apparent attempt at blinding.
Blinding of outcome assessment (detection bias) All outcomes	High risk	No apparent attempt at blinding.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No follow-up on 6/300 participants (not included in analyses)
Selective reporting (reporting bias)	Unclear risk	We did not assess the trial protocol.
Other bias	Low risk	None apparent.

Ganguly 2010

Methods	RCT with randomisation of individual women. Randomisation performed by computer-generated random number list. Opaque sealed envelopes were sequentially numbered. Outcome assessors of the study were blinded
Participants	Inclusion criteria • women with incomplete spontaneous miscarriage diagnosed clinically by passage of some POC and sonographically by endometrial lining exceeding 30 mm and uterine size less than 12 weeks (N = 114) • women with anembryonic gestation or embryonic or fetal death (N = 11) • women with inevitable miscarriage (N = 55)
Interventions	Intervention: vaginal misoprostol • 800 mcg on day 1, second dose of 800 mcg on day 3, if incomplete expulsion • N = 77 Control: surgery • MVA • N = 37
Outcomes	Success (complete uterine evacuation without need for vacuum aspiration for medical management group and without need for repeat aspiration in surgical management group), adverse events, acceptability
Notes	Setting was at RG Kar Medical College and Hospital in Kolkata, India. Study was conducted between 1 May 2007 and 30 April 2008

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated random number list.
Allocation concealment (selection bias)	Low risk	Opaque sealed envelopes with sequence generation and envelope preparation was not involved in the clinical assessment of the subjects
Blinding of participants and personnel (performance bias) All outcomes	High risk	No attempt at blinding.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessors were blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up.
Selective reporting (reporting bias)	Unclear risk	We did not assess the trial protocol.

Ganguly 2010 (*Continued*)

Other bias	Low risk	We did not identify any other biases.

Montesinos 2011

Methods	RCT with randomisation of individual women. Sequentially numbered sealed envelopes, using a computer-generated number allocation. Stratified by site
Participants	Inclusion criteria • Women with incomplete miscarriage (open cervix, vaginal bleeding, uterine size < 12 weeks) • confirmed by ultrasound • N = 242
Interventions	Intervention: oral misoprostol • 600 ug • N = 122 Comparison: surgery • MVA (under general anaesthesia at public hospital, local anaesthesia at private clinic) • N = 120
Outcomes	Primary: completeness of miscarriage at one week (based on questioning about symptoms, pelvic examination +/- ultrasound). Secondary: further treatment, adverse effects, satisfaction
Notes	Two centres in Ecuador: large public tertiary maternity hospital (N = 200), small private clinic (N = 42) Set-up as feasibility study aiming to recruit 500 women. Closed after a year with around half recruited Recruitment 2006-2007.

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated in blocks of 10.
Allocation concealment (selection bias)	Low risk	Sealed numbered envelopes opened after consent.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No attempt at blinding.
Blinding of outcome assessment (detection bias) All outcomes	High risk	No attempt at blinding.

Montesinos 2011 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	High risk	39/242 (16.1%) women did not return for assessment and were not included in analyses
Selective reporting (reporting bias)	Unclear risk	We did not assess the trial protocol.
Other bias	Low risk	We did not identify any other biases.

Moodliar 2005

Methods	RCT with randomisation of individual women. Sequentially numbered sealed envelopes, using a computer-generated number allocation
Participants	Women with spontaneous incomplete miscarriage after up to 13 weeks' gestation assessed by ultrasound N = 94 women
Interventions	Intervention: vaginal misoprostol • 600 ug (plus a second dose 24 hours later if miscarriage still not complete) • N = 47 Comparison: surgery • surgical ERPC by sharp curettage following 20 U of oxytocin per litre of normal saline under GA with no prophylactic antibiotics but oral analgesics were prescribed • N = 47
Outcomes	Women requiring ERPC after failed medical management; number of doses of misoprostol required; duration of bleeding; adverse effect profile (nausea, vomiting and/or diarrhoea); time spent away from work; use of analgesia
Notes	1. Setting: Gynaecology Outpatient Dept, Durban, South Africa. 2. Additional outcomes assessed but not prespecified in the review: Hb at 4 days; pain (VAS); duration of analgesia; days of sick leave; satisfaction (VAS); would use same treatment again; would recommend treatment to friend.

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"Computer-generated patient number allocation."
Allocation concealment (selection bias)	Low risk	"The number was sealed consecutively numbered envelopes by staff not involved in the study. Sealed envelopes were opened and consecutively enrolled women had their allocated treatment. It is not clear, however, whether the envelopes were

Moodliar 2005 (*Continued*)

		opaque or not."
Blinding of participants and personnel (performance bias) All outcomes	High risk	It was not possible to blind women nor clinicians,
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	It was unclear whether assessors were blinded for some of the outcomes
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss of participants nor exclusions reported.
Selective reporting (reporting bias)	Unclear risk	It would appear so although the prespecified outcomes do not match the reported outcomes fully. Also we did not assess the trial protocol
Other bias	Unclear risk	No figures given on baseline data, only reported as "those who were randomised were well matched for demographic and clinical data". Study not stopped early for benefit and no other apparent biases

Ngoc 2005

Methods	RCT with randomisation of individual women.
Participants	Inclusion criteria • Women with incomplete miscarriage • Women of 18 years or older, living or working within 1 hr of the study hospital, no known contraindication to misoprostol and general good health • N = 300 women Exclusion criteria • None specified
Interventions	Intervention: oral misoprostol • 600 ug • N = 150 Comparison: oral misoprostol • 1200 ug (2 x 600 ug, 4 hours apart) • N = 150
Outcomes	Complete evacuation without recourse to surgery; women's satisfaction and acceptability
Notes	1. Setting: large tertiary facility in Ho Chi Minh City in Southern Vietnam. 2. Mean gestational age was 8.1 weeks, so we consider all to be less than 13 weeks' gestation, this was confirmed by personal communication with co-author, J Blum, but

Ngoc 2005 (*Continued*)

	we have emailed the first author to confirm as suggested. 3. Additional outcomes assessed but not prespecified in the review: bleeding; pain/cramps; fever/chills; tolerability; would choose again; would recommend to a friend.

Risk of bias ***Risk of bias***

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"...computer generated random sequence.."
Allocation concealment (selection bias)	Unclear risk	"...opening the next study envelope..."
Blinding of participants and personnel (performance bias) All outcomes	High risk	Although comparing drug doses, because the comparator group were given second dose 4 hours later, this was not blinded from participants nor caregivers
Blinding of outcome assessment (detection bias) All outcomes	High risk	Although comparing drug doses, because the comparator group were given second dose 4 hours later, this was not blinded from participants nor caregivers
Incomplete outcome data (attrition bias) All outcomes	Low risk	5 women lost to follow-up: 1/150 for single-dose and 4/150 for repeat dose. Authors made every effort to contact women, both by phone and visits but unsuccessfully for these 5 women. There were no exclusions reported, although some outcomes were only available on 145 of the women in the double-dose group rather than 146. The analysis was not by ITT because of the lost data, but we considered the loss was small enough for there to be no important bias
Selective reporting (reporting bias)	Unclear risk	Seem to have reported all prespecified outcomes, but we did not access the trial protocol
Other bias	Low risk	There was nothing to suggest any other risk of bias.

Niinimaki 2006

Methods	RCT with randomisation of individual women.
Participants	Inclusion criteria • Women with incomplete spontaneous miscarriage and IUFD, with only women with incomplete miscarriage being included in this review • Women aged > 18 years with positive pregnancy test and with one of the following: in transvaginal ultrasonography an inhomogeneous mass with a diameter of 15-50 mm in the uterine cavity (incomplete spontaneous abortion); empty amnion sac with a diameter of > 15 mm (anembryonic pregnancy); or crown-rump length > 5 mm without signs of fetal heart function (missed abortion). All kinds of miscarriage were included (missed abortion; anembryonic pregnancies; incomplete spontaneous abortion) • N = 19 women (98 were randomised of which 19 had incomplete miscarriage) Exclusion criteria • Women with profuse bleeding; signs of endometritis, allergies to either drug; severe asthma, suspected cases of molar or extrauterine pregnancy
Interventions	Intervention: oral mifepristone + vaginal misoprostol • Oral mifepristone (200 mg) + vaginal misoprostol (800 ug) • N = 11 Comparison: surgery • Curettage • N = 8 • Some women (mainly nulliparous) were given 400 ug vaginal misoprostol 2 hours before to ripen the cervix
Outcomes	Complete abortion rate; bleeding; pain; satisfaction; complications including infection (clinical signs or elevated infection parameters in lab tests) treated with oral or intravenous antibiotics; continuous and heavy bleeding; blood transfusions; curettage for any reason; intense pain requiring admission
Notes	Setting: Oulu University Hospital, Finland. The 19 women with incomplete spontaneous miscarriage were part of a larger study of 98 women who had had various forms of miscarriage (incomplete spontaneous miscarriage; anembryonic pregnancy; missed miscarriage). Separate data were available from the authors for the women with incomplete spontaneous miscarriage. Of the 19 women, 16 were < 13 weeks' gestation and 3 were between 13 and 23 weeks' gestation. This information is held at the Cochrane Pregnancy and Childbirth Office

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"...computer randomised program with the block length of 6."
Allocation concealment (selection bias)	Low risk	"An independent consult performed the randomisation and assigned the randomisation list to a secretary, who made the

		numbered opaque envelopes for the study. ...Allocation concealment was used to confirm that neither the clinician nor the patient knew the type of treatment in advance...After informed consent the next numbered envelope was opened to define the type of treatment of each patient."
Blinding of participants and personnel (performance bias) All outcomes	High risk	Cannot blind women nor clinicians to the treatment because this study compared medical versus surgical treatment
Blinding of outcome assessment (detection bias) All outcomes	High risk	Cannot blind women nor clinicians to the treatment because this study compared medical versus surgical treatment
Incomplete outcome data (attrition bias) All outcomes	Low risk	Authors randomised 98 women (19 with ICM and 79 with IUFD) with 49 in each group. Of these, they reported on 48 in medical and 47 in surgical groups because 1 woman in the medical management group had an ERPC and in the surgical group one woman had an emergency ERPC and one had a spontaneous complete miscarriage. Of these women only 19 had incomplete miscarriage (the remainder had intrauterine deaths) and of these all appear to be accounted for in the analysis
Selective reporting (reporting bias)	Unclear risk	We did not assess the protocol, and additionally the authors did not report on bleeding; blood transfusions
Other bias	Low risk	No apparent additional biases apparent.

Pang 2001

Methods	RCT with randomisation of individual women.
Participants	Inclusion criteria • Women with clinical diagnosis of incomplete miscarriage confirmed by transvaginal ultrasound • Specifically - women with clinical diagnosis of incomplete miscarriage, positive urinary pregnancy test, confirmed by transvaginal ultrasonography (TVS) with evidence of retained POC • N = 201 women Exclusion criteria • Women with an intrauterine dimension measuring < 11 cm^2 (sagittal plus

Pang 2001 (*Continued*)

	transverse plane) were considered to have an empty uterus and excluded from randomisation. Also excluded were women with: severe blood loss; sepsis; known allergy to prostaglandins or analogue, history of asthma, clinician thought unsuitable for misoprostol.
Interventions	Intervention: vaginal misoprostol • 800 ug - 2 doses if necessary • N = 96 Comparison: oral misoprostol • 800 ug - 2 doses if necessary • N = 105
Outcomes	Efficacy; side effects; short-term complications. • outcomes assessed at 1 day following treatment and again at 2 weeks
Notes	1. Setting: The Chinsese University of Hong Kong. 2. Additional outcomes assessed but not prespecified in the review: bleeding; pain; fever; drop in Hb.

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated set of random numbers in blocks of 5.
Allocation concealment (selection bias)	Low risk	Opaque envelopes labelled serially.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information and differing routes of administration suggest there was high risk of performance bias
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information and differing routes of administration suggest there was high risk of detection bias
Incomplete outcome data (attrition bias) All outcomes	High risk	Of the 201 women randomised, 198 got the treatment allocated, but only 186 were analysed because 12 were lost to follow-up - 7.5%. It is unclear whether ITT analysis was undertaken
Selective reporting (reporting bias)	Unclear risk	No obvious outcome reporting bias but authors do not list their outcomes and although only report significant differences in abstract, in paper they report several adverse outcomes with data. We did not assess the trial protocol.

Pang 2001 (*Continued*)

Other bias	Low risk	Significantly more women in oral group had a past history of termination, P < 0. 001, but this was thought to probably not to create important bias

Paritakul 2010

Methods	RCT with randomisation of individual women.
Participants	Inclusion criteria • women with incomplete miscarriage (clinical diagnosis confirmed by ultrasound) attending one hospital in Bangkok, Thailand • N = 64 Exclusion criteria • haemodynamic instability, suspected sepsis, allergy to misoprostol, suspected ectopic pregnancy
Interventions	Intervention: misoprostol sublingually • 600 mcg • N = 32 Comparison: misoprostol orally • 600 mcg • N = 32
Outcomes	Efficacy; side effects; short-term complications. • outcomes assessed at 48 hours following treatment and again at 1 week. 'Treatment failure' was incomplete miscarriage at 48 hours
Notes	

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Sequence generated from random number tables.
Allocation concealment (selection bias)	Low risk	Consecutively numbered, sealed envelopes.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No attempt at blinding of participants or staff.
Blinding of outcome assessment (detection bias) All outcomes	High risk	No attempt at blinding of participants or staff.

Paritakul 2010 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up.
Selective reporting (reporting bias)	Unclear risk	We did not assess the trial protocol.
Other bias	Low risk	We did not identify any other biases.

Patua 2013

Methods	RCT with randomisation of individual women.
Participants	Inclusion criteria • Age 15-45 year with diagnosis of incomplete abortion • Haemodynamically stable • Amenorrhea of less than or equal to 84 days • No prior history of intervention • Spontaneous onset Exclusion criteria • Patients in shock, bleeding profusely, septic abortion • History of previous caesarean section delivery • Contraindication to misoprostol (allergy, asthma) • Women presenting with products hanging from external os which were removed digitally
Interventions	Intervention: vaginal misoprostol • Misoprostol 400 mcg vaginal every 3 hours x 3 doses regardless of POC expulsion • N = 50 Control: surgical • Traditional suction and curettage under deep sedation with 50 mg pethidine injection • N = 50
Outcomes	Primary outcome: success of the procedure = no POC in follow-up scan (24 hours after last dose/surgical evacuation) OR no need for curettage/repeat curettage (failure defined as POC on follow-up scan, necessary surgical evacuation due to retained POC or profuse bleeding following miso administration) Secondary outcome: amount of procedure-related blood loss and side effects The amount of blood loss was measured by the change in haemoglobin percentage and by the number of pads changed in first 24 hours following treatment allocation. Women were asked to change the pads only when the outer surface of the pads got stained Complications related to the procedures were those which could be measured quantitatively (fever, i.e. temperature 100.4 °F) and subjectively (severe pain judged by VAS over 7 on a scale of 1-10)
Notes	Study setting: Department of Gynecology and Obstetrics, Eden Hospital, Medical College, Kolkata, India, in 2009

Risk of bias	***Risk of bias***

Patua 2013 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number table.
Allocation concealment (selection bias)	Unclear risk	Women were allocated to 2 groups using a random number table. No mention of using sealed opaque envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	Double-blinding could not be done as observers were responsible for clinical management of the patients and had to know the treatment that each patient was offered
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Sonographer blinded to intervention or control group.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	4 lost from the intervention group - 1 woman was detected having pre-existing jaundice. Another 1 left the hospital without intimation. 2 refused to continue treatment following administration of the first dose of misoprostol and urged for surgical clearance. All 4 of them were excluded from the study
Selective reporting (reporting bias)	Unclear risk	Protocol not published.
Other bias	Low risk	We did not identify any other biases.

Sahin 2001

Methods	RCT with randomisation of individual women.
Participants	Inclusion criteria • Women with uncomplicated incomplete spontaneous miscarriage assessed with ultrasound • Women with a history of vaginal bleeding, cramping abdominal pain and passage of some products of the conceptus; in good health with a normal Hb level (> 9 g/dL) and haemodynamically stable; estimated gestational age was ≤ 10 weeks, if the anterior-posterior diameter of any retained product of the conceptus was < 50 mm, and if they had no contraindication to prostaglandin treatment • N = 80 women Exclusion criteria • Women with temperature > 37.5 ^{0}C, excessive vaginal bleeding requiring immediate surgical evacuation, haemodynamic instability or foul-smelling products of the conceptus

Sahin 2001 (*Continued*)

Interventions	Intervention: oral + vaginal misoprostol • 200 ug 4 times daily after application of 200 ug intravaginal misoprostol for 5 days • N = 40 Comparison: surgical management • Curettage, sometimes with general anaesthesia • N = 40
Outcomes	Number of days of vaginal bleeding; rate of complications (fall in Hb, infection, perforation) and women's satisfaction • Miscarriage assessed at 10 days but no indication on whether this was a clinical assessment or by ultrasound
Notes	1. Setting: University hospital, Turkey. 2. Additional outcomes assessed but not prespecified in the review: mean change in Hb; dissatisfaction.

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No information provided, except to say women were randomised
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Neither participants nor clinicians can be blinded.
Blinding of outcome assessment (detection bias) All outcomes	High risk	There is no mention as to whether the outcome assessor was blinded. For outcomes where participants assessed for themselves, these were not blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No losses and no exclusions were reported, but nothing is described. As there is no deviation from protocol it is assumed that analysis was by ITT
Selective reporting (reporting bias)	Unclear risk	Seem to report on all outcomes specified in 'Materials and methods' but we did not assess the trial protocol
Other bias	Unclear risk	No imbalances in baseline data identified (assessed: age, gravity, parity, gestational age, anterior-posterior diameter). Study not stopped early and no apparent differential diagnosis

Shelley 2005

Methods	RCT with randomisation of individual women. Used a centralised computer-based enrolment and randomisation service. The Co-ordinating Centre used the biased coin method of maintaining balance between study arms, and was stratified by hospital and gestation (< 7 weeks; 8-10 weeks; 11-13 weeks)
Participants	Inclusion criteria • Women with incomplete or inevitable miscarriage at < 13 weeks' gestation assessed clinically • Bleeding not excessive, haemodynamic system stable, temperature < 37.5 ^{0}C, no history of current serious systemic medical or surgical condition, use of prostaglandins not contraindicated (allergy, mitral stenosis, diabetes, blood dyscrasia, haemolytic disease, glaucoma, sickle cell anaemia, hypertension, epilepsy or severe asthma), 18 years or older, not taking anticoagulants or oral corticosteroids, singleton pregnancy, no intrauterine device in situ, and sufficient familiarity with English to complete written questionnaires • N = 40 women Exclusion criteria • A non-viable intrauterine pregnancy diagnosed on ultrasound but with no vaginal bleeding
Interventions	Intervention 1: vaginal misoprostol • 400u g with repeat dose 4-6 hours later if needed (= 400 ug or 800 ug) • N = 13 but 1 woman withdrew immediately after randomisation leaving. N = 12 Intervention 2: surgical management • Aspiration curettage or D&C under GA • N = 12 Comparison: expectant care • N = 15
Outcomes	Successful evacuation; infection; haemorrhage; pain; bleeding; physical and emotional recovery; anxiety and depression • Assessed clinically at 10-14 days and 8 weeks
Notes	1. Setting: 5 metropolitan hospitals, Melbourne, Australia. 2. Additional outcomes assessed but not prespecified in the review: pain; return to usual activities after 2 and 6 days; HADS anxiety score at 2 and 6 days; would choose this method again.

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"...a centralised computer-based enrolment and randomisation service...using the biased coin method of maintaining balance between study arms, and was stratified by hospital and gestation (7 weeks or less, 8 - 10 weeks, 11 - 13 weeks)."

Shelley 2005 (*Continued*)

Allocation concealment (selection bias)	Low risk	"...a centralised computer-based enrolment and randomisation service, available by telephone 24 hours a day."
Blinding of participants and personnel (performance bias) All outcomes	High risk	"Participants and clinicians could not be blinded."
Blinding of outcome assessment (detection bias) All outcomes	High risk	Unclear if outcome assessor blind or not, although not for outcomes assessed by women. Reports that "The data analyst had access to unblinded data but no contact with any study participant."
Incomplete outcome data (attrition bias) All outcomes	Low risk	One woman randomised to medical prescription (misoprostol) withdrew following randomisation and was not included in the analyses Medical group: 1 woman was lost to follow-up at 10 to 14 days; 1 woman was lost to follow-up at 8 weeks Surgical group: 1 woman was lost to follow-up at 8 weeks. Expectant group: 1 woman was lost to follow-up at 8 weeks.
Selective reporting (reporting bias)	Unclear risk	Outcome measures are listed in the methods section and are those reported in the results section. We did not assess the trial protocol
Other bias	Low risk	Study was planned to recruit 831 women from power calculation 80% power to detect of 5% (99% to 91%) at 0.05 level, but staff were recruiting < 50% eligible women and of these only 22% agreed. So, in effect stopped early but not because of benefit, so probably no bias, just underpowered. No data provided on baseline balance, but reported that: "there were no marked or systematic differences between the groups at trial entry with regards to gestation, women's age, reproductive history, methods of diagnosis, days of bleeding, pain, haemoglobin or white cell count." There seemed to be no differential diagnosis.

Shochet 2012

Methods	RCT with randomisation of individual women.
Participants	Inclusion criteria • Eligible incomplete abortion = past or present history of vaginal bleeding during pregnancy and an open cervical os (if ultrasound not used) or evidence of incomplete abortion with substantial debris in uterus, if ultrasound used • Uterine site no larger than 12 weeks • No contraindications to study drug • No severe infection • No haemodynamic disturbances • General good health • Willing to provide contact info for follow-up purposes Exclusion criteria • Suspicion of ectopic pregnancy
Interventions	Intervention: sublingual misoprostol • Misoprostol 400 mcg sublingual x 1 dose • N = 480 Comparison: surgical evacuation • Surgical evacuation per standard practice of each hospital (MVA or D&C) • N = 380
Outcomes	Primary: complete abortion at follow-up (success) • Follow-up in 1 week; if incomplete, given a choice of additional week follow-up or surgical evacuation; if still incomplete at 2nd follow-up, underwent surgical evacuation • Diagnosis assessed by clinical exam and in event of continued heavy bleeding, enlarged uterus, or suspicion of ectopic pregnancy, referred for ultrasound Additional outcomes: side effects, acceptability.
Notes	Study setting: data from 1 multi-site (Mauritania, Niger, and Senegal) and 2 country-level (Burkina Faso and Nigeria) randomised trials comparing sublingual misoprostol to standard surgical care for treatment of incomplete abortion were combined. Study sites were located in Guédiawaye, Senegal; Nouakchott, Mauritania; Niamey, Niger; Ibadan, Nigeria; and Ouagadougou and Bobo Dioulasso, Burkina Faso

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No details of randomisation.
Allocation concealment (selection bias)	Unclear risk	No details given.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No details given.

Shochet 2012 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No details given. Use of ultrasound to determine outcome was more likely to occur with women in the misoprostol arm than with those in the surgical arm
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	15 in intervention and 6 in MVA group - no information on whether this group Is different
Selective reporting (reporting bias)	Unclear risk	Protocol not published.
Other bias	Low risk	We did not identify any other biases.

Shwekerela 2007

Methods	RCT with randomisation of individual women in blocks of 10.
Participants	Inclusion criteria • Women with incomplete spontaneous or induced miscarriage, less than 12 weeks' gestation • Women living within 1 hour of hospital; past or present history of bleeding during this pregnancy; cervical os open by visual/digital inspection; uterine size of no greater than 12 weeks since last menstrual period; generally in good health; willing to return for follow-up • N = 300 women Exclusion criteria • Women with severe infection; known allergy to misoprostol; signs of severe infection (foul-smelling discharge, fever > 39 ^{o}C, or pulse > 110/minute) or a known allergy to misoprostol
Interventions	Intervention: oral misoprostol • 600 ug single-dose • N = 150 Comparison: surgery • MVA • N = 150
Outcomes	Successful miscarriage; adverse effects; women's satisfaction • Study protocol did not call for routine ultrasonography either for initial diagnosis or for determination of treatment success • Assessment at 1 week
Notes	1. Setting: Kagera Regional Hospital, Bukoba, Tanzania. 2. All women observed for 3 hours after prescription before being allowed home and antibiotics were given as needed. If miscarriage still incomplete at 7 days, women offered additional week or MVA. Any woman still with incomplete miscarriage at 14 days was offered MVA.

	3. Additional outcomes assessed but not prespecified in the review: bleeding; pain; fever; tolerability.

Risk of bias ***Risk of bias***

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"....computer-generated random code, created in bocks of 10 at Genunity Health Projects' Office in New York City."
Allocation concealment (selection bias)	Low risk	"The code was used by a Genunity employee who was not part of the research team as a basis for sealing cards in consecutively numbered envelopes... staff would open the next envelope in the numbered series...". Although not opaque enveloped, we think the numbered series should be alright
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not able to blind participants or clinicians.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not able to blind participants or clinicians.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up and no deviations from protocol allocation reported. ITT analysis
Selective reporting (reporting bias)	Unclear risk	Report on prespecified outcomes, although we have not assessed the trial protocol
Other bias	Low risk	On most characteristics, women did not differ significantly. But significantly more women in the misoprostol group had spontaneous miscarriage and were married. However, we considered that this probably will not have any impact on differences in outcome

Taylor 2011

Methods	Randomised controlled trial.
Participants	Inclusion criteria • Women with incomplete miscarriage (clinical diagnosis - vaginal bleeding, open cervix, uterus < 12 week size. • Sometimes confirmed by ultrasound; attending one regional hospital in Ghana • N = 229 Exclusion criteria • Suspected sepsis (temperature > 38), allergy to misoprostol
Interventions	Intervention: oral misoprostol • 600 mcg • N = 113, but 108 analysed Comparison: surgery • MVA • N = 116, but 110 analysed
Outcomes	Efficacy; side effects; short-term complications. • Outcomes assessed at 7 days following treatment. 'Treatment failure' was incomplete miscarriage at 1 week
Notes	

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated random sequence in blocks of 10.
Allocation concealment (selection bias)	Low risk	Sealed sequential envelopes.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No attempt at blinding.
Blinding of outcome assessment (detection bias) All outcomes	High risk	No attempt at blinding.
Incomplete outcome data (attrition bias) All outcomes	Low risk	11/229 women lost to follow-up.
Selective reporting (reporting bias)	Unclear risk	We did not assess the trial protocol.
Other bias	Low risk	We did not identify any other biases.

Trinder 2006

Methods	RCT with randomisation of individual women. Randomisation was by a central telephone system at the Clinical Trials Unit using minimisation to ensure comparability
Participants	Inclusion criteria • Women of less than 13 weeks' gestation with a diagnosis of either incomplete miscarriage or early fetal/embryonic demise • Defined ICM as areas of mixed echogenicity within the uterine cavity with or without a disordered gestational sac. Early embryonic demise was defined as an intact gestational sac of greater than 20 mm mean diameter with no other internal structures and early fetal demise as a fetus over 6 mm crown rump length with no heart activity on transvaginal ultrasound scan • N = 1200 women. Incomplete miscarriage N = 274; early fetal demise N = 924 Exclusion criteria • Women with severe haemorrhage or pain; pyrexia > 38^{o}C; severe asthma; haemolytic disease or blood dyscrasias; current anticoagulation or systemic corticosteroid prescription; twin or higher order pregnancy; smoker aged > 35; inability to understand English
Interventions	Intervention 1: vaginal misoprostol • 800 ug • N = 398 total; ICM = 90; IUFD = 308 Intervention 2: surgery • Suction curettage • N = 403 total; ICM = 92; IUFD = 310 Comparison: expectant care • N = 399 total; ICM = 92; IUFD = 306 All women were given a specific information sheet, 30 co-dydramol tablets, and an emergency telephone number
Outcomes	Primary outcome: gynaecological infection within 14 days of trial entry Secondary outcomes: antibiotics for presumed gynaecological infection within 14 days and within 8 weeks; duration of clinical symptoms (pain, additional analgesia, vaginal bleeding; days off work, days before return to usual daily activities); complications (fall in Hb at 10-14 days, blood transfusion, unplanned consultations or admission within 14 days and within eight weeks); efficacy; psychological outcomes (depression and anxiety) ; and return to normal activity • Unplanned curettage assessed at 2 weeks and 8 weeks
Notes	1. Setting: early pregnancy assessment unit in 7 hospitals in UK. 2. Results are reported by both IUFD and ICM. However, randomisation was not reported as stratified so there will be risk of bias in using data from the subgroups. 3. Additional outcomes assessed but not prespecified in the review: none.

Risk of bias		***Risk of bias***
Bias	**Authors' judgement**	**Support for judgement**

Random sequence generation (selection bias)	Low risk	"Randomisation was by a central telephone system at the Clinical Trials Unit in Oxford. We used minimisation to ensure comparability between women with respect to participating centres, parity, type of miscarriage and gestation."
Allocation concealment (selection bias)	Low risk	Randomisation was by a central telephone system at the Clinical Trials Unit in Oxford, and although no specific information given on randomisation, clinical trials units generally use computer-generated random numbers list
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible to blind women nor clinicians, because women given medical or surgical intervention were treatment in hospital and women in expectant arm were able to go home. Cannot blind surgery versus medical treatment or expectant care.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not possible to blind women nor clinicians, because women given medical or surgical intervention were treatment in hospital and women in expectant arm were able to go home. Cannot blind surgery versus medical treatment or expectant care.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Loss of participants to follow-up: • loss immediately after randomisation: misoprostol = 0; surgery = 1; expectant care = 1. • loss at 14-day outcomes; misoprostol = 9 ; surgery = 8; expectant care = 5. • loss at 8-week outcomes: misoprostol = 3; surgery = 2; expectant care = 6. However, we do not know whether these women had ICM or IUFD, but at a maximum loss would be 10%. Exclusions after randomisation: In each of the surgical group and expectant care group, one woman with a viable pregnancy was excluded. Analysis was by ITT
Selective reporting (reporting bias)	Unclear risk	All important prespecified outcomes were reported, but we have not assessed the trial protocol

Trinder 2006 (*Continued*)

Other bias	Unclear risk	Study stopped early because struggling to recruit and not because of benefit, so bias unlikely. There were no important baseline differences between the 3 groups However, the randomisation was not reported as stratified by women with ICM and women with IUFD and so these may not have similar groups for comparison

Weeks 2005

Methods	RCT with randomisation of individual women. Consecutively numbered sealed opaque envelopes, using a computer-generated random number
Participants	Inclusion criteria • Women with incomplete miscarriage of less than 13 weeks' gestation • Clinical diagnosis • N = 317 women Exclusion criteria • Women presenting with haemorrhage causing haemodynamic changes; ay suspicion of an ectopic pregnancy, severe asthma, signs of severe infection, known sensitivity to misoprostol
Interventions	Intervention: oral misoprostol • 600 ug • N = 160 Comparison: surgery • MVA • Women given 50 mg pethidine and 0.2 mg ergometrine • N = 152
Outcomes	Completeness of evacuation; adverse effects, maximum pain and blood loss • Clinical assessment at 7 days
Notes	1. Setting: Mulago Hospital, Kampala, Uganda. 2. On discharge all women given doxycycline (100 mg/12 hours for 7 days) and metronidazole (400 mg 3 times a day for 5 days) because of the high incidence of septic abortion in Urganda. 3. Additional outcomes assessed but not prespecified in the review: severity of bleeding; maximum pain; adverse effects; satisfaction; would choose method again; would recommend to a friend; worst and best aspects of treatment. 4. Poor response in terms of women not returning for follow-up appointment happened despite transport costs being provided.

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**

Weeks 2005 (*Continued*)

Random sequence generation (selection bias)	Low risk	"Computer-generated random numbers... "
Allocation concealment (selection bias)	Low risk	"The allocation was written on cards and placed in consecutively numbered opaque sealed envelopes."
Blinding of participants and personnel (performance bias) All outcomes	High risk	"Neither the patients, assessors, nor the data analysers were blinded to the allocation." It was not possible to blind women or clinicians because a drug was compared with surgery.
Blinding of outcome assessment (detection bias) All outcomes	High risk	"Neither the patients, assessors, nor the data analysers were blinded to the allocation." It was not possible to blind women or clinicians because a drug was compared with surgery.
Incomplete outcome data (attrition bias) All outcomes	High risk	Loss of participants to follow-up from 317 women randomised was considerable and was discussed by authors. Many women in the rural communities of Uganda did not come for follow-up after discharge. • At 6 days - no loss to follow-up. • At 1-2 weeks: Misop had 53/160 (33%) lost to follow-up - leaving 107 women. • MVA had 70/157 (45%) lost to follow-up - leaving 82 women. 5 women were excluded in the MVA group (3 for self-discharge and 2 women were incorrectly excluded by the recruiter after randomisation but before treatment, 1 because she did not fit the entry criteria and 1 because no manual vacuum aspiration kit was available) • One woman in misoprostol group and 7 in MVA group were given the wrong prescription, but were included on ITT for analysis. • Included in MVA were 6 women for whom MVA was not possible (5 amount of retained products too great and 1 the os had closed). The study was analysed by ITT based on available data.

Weeks 2005 (*Continued*)

Selective reporting (reporting bias)	Unclear risk	Seem to report findings fully, there is just the problem of large losses to follow-up - due to the low-income country setting probably. We have not assessed the trial protocol.
Other bias	Unclear risk	Study was stopped for pragmatic reasons and not for benefit (principle investigator moved) and os; probably no bias Clinical characteristics at presentation were similar between the 2 groups, although no P values reported Women in the MVA group were given routine analgesia, where women in the medical management group had analgesia on request. However, women in MVA still had more pain, so pain with MVA likely to be underestimated

Zhang 2005

Methods	RCT with randomisation of individual women in ratio of 3:1.
Participants	Inclusion criteria • Women with incomplete miscarriage and intrauterine fetal death • Women with anembryonic gestation or embryonic or fetal death, also women with incomplete or inevitable miscarriage, were enrolled in the trial after assessment using ultrasound • N = 652 total; ICM - N = 39; IUFD - N = 613 Exclusion criteria • Women with anaemia (< 9.5 g/dL); haemodynamic instability; history of clotting disorder; using anticoagulants (not including aspirin); allergic to prostaglandins or non-steroidal anti-inflammatory drugs; previously undergone surgical or medical abortion either self-induced or induced by other physicians during this pregnancy.
Interventions	Intervention: vaginal misoprostol • 800 ug (4 x 200 ug) • N = 30 Comparison: surgery • Vacuum aspiration • N = 9
Outcomes	Success, Hb, fever, nausea, vomiting, diarrhoea, and acceptability • Complete miscarriage assessed at 3 days and 8 days using transvaginal ultrasound
Notes	1. Setting: 4 university settings in US: Columbia University; University of Miami; University of Pennsylvania; University of Pittsburgh. 2. Authors sent us data which separated the outcomes for women with incomplete

	miscarriage and those with intrauterine fetal deaths. 3. Additional outcomes assessed but not prespecified in the review: pain; hospital admission; fever. One additional paper (Harwood 2008) compared women's assessment of quality of life between vaginal misoprostol and surgery. 4. It was reported in the Harwood 2008 publication on this study that despite reporting greater pain and lower acceptability of treatment-related symptoms, quality of life and treatment acceptability were similar for medical and surgical treatments. Here women with incomplete miscarriage and intrauterine deaths were assessed together.

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"...centralised, computer-automated telephone response system..." used to randomly assign women to groups in a 3:1 ratio
Allocation concealment (selection bias)	Low risk	A centralised, computer-automated telephone response system. It was considered that because it was an automated computer response, then allocation concealment would be good
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible to blind either women or clinicians.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not possible to blind either women or clinicians.
Incomplete outcome data (attrition bias) All outcomes	Low risk	One woman lost to follow-up in the surgical group.
Selective reporting (reporting bias)	Unclear risk	Assessed all the prespecified outcomes from the paper, but the trial protocol was not assessed
Other bias	Unclear risk	No significant difference in baseline data reported on the criteria assessed, but difficult to say anything about all other types of bias

D&C: dilation and curettage
ERPC: evacuation of retained products of conception
GA: general anaesthetic
Hb: haemoglobin

ICM: incomplete miscarriage
ITT: intention-to-treat
IUFD: intrauterine fetal death
LMP: last menstrual period
MVA: manual vacuum aspiration
POC: product of conception
RCT: randomised controlled trial
SD: standard deviation
US: ultrasound
VAS: visual analogue scale

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Abd-El-Maeboud 2012	Participants were women with missed miscarriage.
Abdel 1997	Participants were women with an intrauterine fetal death.
Al Inizi 2003	Participants were women with an intrauterine fetal death.
Al-Bdour 2007	Participants were women with an intrauterine fetal death.
Almog 2005	Participants were women having a termination of pregnancy.
Altaf 2006	Mixed group of missed miscarriage, incomplete miscarriage, and termination of pregnancy for other reasons
Amjad 1999	Participants were women with an intrauterine fetal death.
Anderman 2000	Participants were women with an intrauterine fetal death.
Anderson 2009	Medical treatment for non-viable pregnancies.
Ara 2009	Medical treatment for non-viable pregnancies.
Autry 1999	Participants were women with an intrauterine fetal death.
Avila-Vergara 1997	Participants were women with an intrauterine fetal death.
Ayudhaya 2006	Participants were women with an intrauterine fetal death.
Azra 2007	Termination of pregnancy for various reasons.
Bagratee 2004	Study included women with ICM and women with IUFD. We have tried to contact the authors to ask if they could provide their data spilt by women with ICM and women with IUFD. To date we have not had a response

(*Continued*)

Bani-Irshaid 2006	Participants were women having a termination of pregnancy.
Bebbington 2002	Participants were women having a termination of pregnancy.
Behrashi 2008	Participants were women having a termination of pregnancy.
Ben-Meir 2009	Participants mainly undergoing termination of pregnancy. Some with "late missed abortions"
Biswas 2007	Participants were women having a termination of pregnancy.
Cabrol 1990	Participants were women with an intrauterine fetal death.
Caliskan 2005	Participants were women having a termination of pregnancy.
Caliskan 2009	Participants were women having a second trimester termination of pregnancy, some of whom had an intrauterine fetal death
Chittacharoen 2003	Participants were women having a termination of pregnancy.
Chung 1999	Study included women with ICM and women with IUFD. We contacted the authors who were extremely helpful and did provide additional data which are held at the Pregnancy and Childbirth editorial office. However, unfortunately they could not provide their data split by women with ICM and women with IUFD so we were unable to include their data in this review
Cleeve 2015	A RCT comparing groups by provider type.
Creinin 1997	Participants were women with an intrauterine fetal death.
David 2003	Participants were women with an intrauterine fetal death.
David 2005	Participants were women with an intrauterine fetal death.
de Jonge 1995	Quasi-RCT.
Demetroulis 2001	Study included women with ICM and women with IUFD. We have contacted the authors who have tried to help us but are unable to separate their data by women with ICM and women with IUFD
Dickinson 1998	Participants were women having a termination of pregnancy, including some with intrauterine fetal death
Dickinson 2002	Participants were women having a termination of pregnancy, including some with intrauterine fetal death
Dickinson 2003	Participants were women having a termination of pregnancy for fetal abnormality
Egarter 1995	Participants were women with an intrauterine fetal death.

(*Continued*)

Elhassan 2008	Participants were women having a termination of pregnancy, including some with intrauterine fetal death
Eng 1997	Participants were women with an intrauterine fetal death in the 2nd trimester
Eppel 2005	Participants were women having a termination of pregnancy in the 2nd trimester, including some with intrauterine fetal death
Fadalla 2004	Participants were women having a termination of pregnancy in the 2nd trimester, including some with intrauterine fetal death
Fang 2009	Participants were women with an intrauterine fetal death.
Feldman 2003	Participants were women having a termination of pregnancy in the 2nd trimester, including some with intrauterine fetal death
Fiala 2005	Participants were women having a termination of pregnancy for fetal malformations and socioeconomic reasons
Gazvani 2000	Study was of women with incomplete miscarriage, but it assessed surgery versus expectant care, rather than medical management
Ghorab 1998	Participants were women having a termination of pregnancy for fetal malformations or intrauterine fetal death
Gilles 2004	Participants were women with an intrauterine fetal death.
Gonzalez 2001	Participants were women having a termination of pregnancy for intrauterine fetal death or medical or genetic reasons
Graziosi 2004	Participants were women with an intrauterine fetal death.
Grimes 2005	Participants were women having a termination of pregnancy, including some with intrauterine fetal death
Gronlund 2002	Not a RCT, but a prospective cross-over study by alternate regimes every 4 months
Guix 2005	Participants were women having a termination of pregnancy. Also allocated to different treatments at the discretion of the clinician, so not a RCT
Hassan 2007	Quasi-RCT, women allocated to groups based on alternate sequence
Hausler 1997	Participants were women with complete spontaneous miscarriage and endometrial width up to 8 mm
Heard 2002	Participants were women with an intrauterine fetal death.
Herabutya 1997a	Participants were women with an intrauterine fetal death.

(*Continued*)

Herabutya 1997b	Participants were women with an intrauterine fetal death.
Herabutya 2005	Participants were women having a termination of pregnancy.
Hernandez-Valencia 2003	Participants were women with an intrauterine fetal death.
Hidar 2001	Participants were women having a termination of pregnancy.
Hidar 2005	Participants were women having a termination of pregnancy for intrauterine fetal death
Hill 1991	Participants were women with an intrauterine fetal death.
Hinshaw 1997	Study included women with ICM and women with IUFD. We have tried to contact the authors to ask if they could provide their data spilt by women with ICM and women with IUFD. To date we have not had a response
Hogg 2000	Participants were women having a termination of pregnancy, with some for intrauterine fetal death but mostly for fetal anomalies
Hombalegowda 2015	Reference refers to a conference abstract.
Igogo 2015	Reference refers to a conference abstract.
IRCT138902053797N1	Trial of techniques for termination of pregnancy for various reasons
Islam 2006	Participants were women with an intrauterine fetal death.
Jabir 2009	Randomised trial of medical treatments to ripen the cervix before surgical evacuation of the uterus
Jain 1994	Participants were women having a termination of pregnancy for intrauterine fetal death
Jain 1996	Participants were women having a termination of pregnancy for intrauterine fetal death or fetal anomalies
Jain 1999	Participants were women having a termination of pregnancy.
Johnson 1997	Study included women with ICM and women with IUFD. We have tried to contact the authors to ask if they could provide their data spilt by women with ICM and women with IUFD. To date we have not had a response
Kaluaarachchi 2015	Reference refers to a conference abstract.
Kanhai 1989	Participants were women with an intrauterine fetal death.
Kapp 2007	Participants were women having a termination of pregnancy, including women with an intrauterine fetal death
Kara 1999	Participants were women with an intrauterine fetal death.

(*Continued*)

Klingberg 2015	A RCT comparing groups by provider type.
Klingberg-Allvin 2015	A RCT comparing groups by provider type.
Kong 2013	Study included women with ICM and women with IUFD. We have tried to contact the authors to ask if they could provide their data spilt by women with ICM and women with IUFD. To date we have not had a response
Kovavisarach 2002	Participants were women with an intrauterine fetal death.
Kovavisarach 2005	Participants were women with an intrauterine fetal death.
Kushwah 2009	Participants were women with an intrauterine fetal death.
Kushwah 2011	Participants were women with an intrauterine fetal death.
Lelaidier 1993	Participants were women with an intrauterine fetal death.
Lippert 1978	Not a RCT. Women were divided into 2 groups.
Lister 2005	Participants were women with an intrauterine fetal death.
Louey 2000 [pers comm]	Study included women with ICM and women with IUFD. We have tried to contact the authors to ask if they could provide their data spilt by women with ICM and women with IUFD. To date we have not had a response
Lu 2014	Participants were women with missed miscarriage.
Lughmani 2008	Participants were women with an intrauterine fetal death.
Machtinger 2004	Study included women with ICM and women with IUFD. We have tried to contact the authors to ask if they could provide their data spilt by women with ICM and women with IUFD. To date we have not had a response
Makhlouf 2003	Participants were women having a termination of pregnancy.
Martin 1955	Not a RCT; alternate allocation.
Moran 2005	Medical treatment of 'pregnancies of undetermined location'.
Mostafa-Gharebaghi 2010	Termination of pregnancy.
Muffley 2002	Participants were women with an intrauterine fetal death.
Mulayim 2009	Participants were women with an intrauterine fetal death and some having a termination of pregnancy
Nakintu 2001	Participants were women with an intrauterine fetal death.

(*Continued*)

Nasreen 2009	Participants were women with non-viable pregnancies.
NCT00141895	Participants were women with an intrauterine fetal death.
NCT00190294	Participants were women with an intrauterine fetal death.
NCT00468299	Participants were women with an intrauterine fetal death.
Ng 2015	A RCT comparing inpatient versus outpatient treatment.
Ngai 2001	Study included women with ICM and women with IUFD. We have tried to contact the authors to ask if they could provide their data spilt by women with ICM and women with IUFD. To date we have not had a response
Ngoc 2004	Participants were women with an intrauterine fetal death, classified as 'missed abortion'
Nielsen 1999	Study included women with ICM and women with IUFD. We have tried to contact the authors to ask if they could provide their data spilt by women with ICM and women with IUFD. To date we have had no response but we are still trying to contact the authors using a different email address
Niromanesh 2005	Participants were women with an intrauterine fetal death.
Nor Azlin 2006	Participants were women having a termination of pregnancy, including women with an intrauterine fetal death
Nuthalapaty 2005	Participants were women having a termination of pregnancy, including women with an intrauterine fetal death
Nuutila 1997	Participants were women having a termination of pregnancy, including women with an intrauterine fetal death
Owen 1999	Participants were women with indication for termination of pregnancy
Pansky 2011	Pilot RCT of Intercoat gel versus control for proventing adhesion
Paraskevaides 1992	Included both women with incomplete miscarriage and women with intrauterine fetal death. We were unable to contact the authors to request split data
Perry 1999	Participants were women with indication for termination of pregnancy
Petersen 2013	Study included women with ICM and women with IUFD. We contacted the authors who were extremely helpful and did provide additional data. However, unfortunately they could not provide their data split by women with ICM and women with IUFD so we were unable to include their data in this review
Piotrowski 1979	Participants were women with an intrauterine fetal death.
Pongsatha 2004	Participants were women with indication for termination of pregnancy

(*Continued*)

Ramsey 2004	Participants were women with indication for termination of pregnancy
Rausch 2012	Secondary analysis of study that included women with both incomplete miscarriages and non-viable pregnancies
Rita 2006	Participants were women with an intrauterine fetal death.
Rivero-Lopez 1998	Participants were women with an intrauterine fetal death.
Roy 2003	Participants were women with indication for termination of pregnancy
Ruangchainikhom 2006	Participants were women with indication for termination of pregnancy
Saichua 2009	Participants were women with an intrauterine fetal death.
Salamalekis 1990	Not a RCT; no mention of randomisation.
Sathapanachai 2000	Participants were women with an intrauterine fetal death.
Shah 2010	Participants were women with an intrauterine fetal death.
Shaikh 2008	Participants were combined group women with an intrauterine fetal death and those with miscarriage. Abstract only
Shobeira 2007	Participants were women with an intrauterine fetal death.
Shokry 2009	Trial of misoprostol after evacuation of uterus to try to decrease blood loss
Shuaib 2013	Participants were women with missed miscarriage.
Sonsanoh 2014	Participants were women with missed miscarriage.
Sripramote 2000	Trial of misoprostol to prime cervix before routine surgical uterine evacuation
Stockheim 2006	Participants were women with an intrauterine fetal death.
Su 2005	Participants were women with indication for termination of pregnancy
Suchonwanit 1999	Participants were women with an intrauterine fetal death.
Surita 1997	Participants were women with an intrauterine fetal death.
Tang 2003	Participants were women with 'silent miscarriage' and women with complete and incomplete miscarriages were excluded
Tang 2006a	Participants were women with 'silent miscarriage' and women with incomplete miscarriages were excluded

(*Continued*)

Tanha 2010	Trial of treatment for non-viable pregnancies.
Thavarasah 1986	Participants were women with an intrauterine fetal death.
Thida 2015	Reference refers to a conference abstract.
Toppozada 1994	Participants were women with indication for termination of pregnancy for intrauterine fetal death
Torre 2012	Trial of treatment for combined incomplete miscarriages and non-viable pregnancies
Wood 2002	Participants were women with an intrauterine fetal death.
Yapar 1996	Participants were women with indication for termination of pregnancy including women with intrauterine fetal death
Yilmaz 2005	Participants were women with indication for termination of pregnancy including women with intrauterine fetal death
Yilmaz 2007	Participants were women having termination of pregnancy, some of whom had an intrauterine fetal death
Yu 2000	Participants were women with missed miscarriage.
Zhang 2000	Study of techniques of induction of labour.

ICM: incomplete miscarriage
IUFD: intrauterine fetal death
RCT: randomised controlled trial

Characteristics of ongoing studies *[ordered by study ID]*

ISRCTN65305620

Trial name or title	Is misoprostol a safe alternative to manual vacuum aspiration in women with incomplete abortions in developing countries?
Methods	Evaluator-blinded, single-centre, randomised controlled non-inferiority trial
Participants	Women with first trimester pregnancy loss
Interventions	Intervention: sublingual misoprostol - 600 mcg (3 doses of 200 ug each every 4 hours) Comparison: surgery (MVA)
Outcomes	Ultrasonagraphic thickness; change in Hb; pain; adverse effects; women's satisfaction and acceptability

ISRCTN65305620 (*Continued*)

Starting date	11 February 2008
Contact information	Dr Regina Unkels, PO Box 97, Lindi, Tanzania
Notes	Study No: ISRCTN65305620 Website: www.tgpsh.or.tz

NCT01033903

Trial name or title	Which is the optimal treatment for miscarriage with a gestational sac in the uterus and which factors can predict if the treatment will be successful?
Methods	Open-label, randomised controlled trial
Participants	Women with incomplete miscarriage before 14 weeks and a gestational sac retained in the uterus
Interventions	Intervention: misoprostol 800 mcg intravaginally once Comparison: expectant management
Outcomes	Primary outcome: complete miscarriage at 10 day follow-up Secondary outcome: complete miscarriage at 17 days, 24 days, 31 days follow-up
Starting date	October 2008
Contact information	Contact information no longer displayed due to end of recruitment
Notes	Location: Sweden Study identifier: NCT01033903

Hb: haemoglobin
MVA: manual vacuum aspiration

DATA AND ANALYSES

Comparison 1. Misoprostol versus expectant care

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Complete miscarriage	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 Vaginal misoprostol	2	150	Risk Ratio (M-H, Random, 95% CI)	1.23 [0.72, 2.10]
1.2 Oral misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 Vaginal + oral misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 Rectal misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
1.5 Sublingual misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2 Surgical evacuation	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 Vaginal misoprostol	2	308	Risk Ratio (M-H, Random, 95% CI)	0.62 [0.17, 2.26]
2.2 Oral misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2.3 Vaginal + oral misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2.4 Rectal misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2.5 Sublingual misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
3 Death or serious complication	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 Vaginal misoprostol	1	126	Risk Ratio (M-H, Random, 95% CI)	2.91 [0.12, 70.05]
3.2 Oral misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
3.3 Vaginal + oral misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
3.4 Rectal misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
3.5 Sublingual misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
4 Unplanned surgical intervention	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
4.1 Vaginal misoprostol	2	308	Risk Ratio (M-H, Random, 95% CI)	0.62 [0.17, 2.26]
4.2 Oral misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
4.3 Vaginal + oral misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
4.4 Rectal misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
4.5 Sublingual misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5 Blood transfusion	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
5.1 Vaginal misoprostol	3	332	Risk Ratio (M-H, Random, 95% CI)	3.07 [0.13, 74.28]
5.2 Oral misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5.3 Vaginal + oral misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5.4 Rectal misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5.5 Sublingual misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6 Pain relief	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
6.1 Vaginal misoprostol	2	308	Risk Ratio (M-H, Random, 95% CI)	1.12 [0.67, 1.88]
6.2 Oral misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6.3 Vaginal + oral misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6.4 Rectal misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6.5 Sublingual misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7 Pelvic infection < 14 days	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
7.1 Vaginal misoprostol	3	333	Risk Ratio (M-H, Random, 95% CI)	2.42 [0.59, 9.98]
7.2 Oral misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.3 Vaginal + oral misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.4 Rectal misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.5 Sublingual misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Comparison 2. Misoprostol versus surgery

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Complete miscarriage	15	3862	Risk Ratio (M-H, Random, 95% CI)	0.96 [0.94, 0.98]
1.1 Vaginal misoprostol	5	364	Risk Ratio (M-H, Random, 95% CI)	0.90 [0.85, 0.95]
1.2 Oral misoprostol	7	1884	Risk Ratio (M-H, Random, 95% CI)	0.98 [0.95, 1.00]
1.3 Vaginal + oral misoprostol	1	80	Risk Ratio (M-H, Random, 95% CI)	0.95 [0.87, 1.04]
1.4 Rectal misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
1.5 Sublingual misoprostol	2	1534	Risk Ratio (M-H, Random, 95% CI)	0.97 [0.92, 1.01]
2 Surgical evacuation	13	3070	Risk Ratio (M-H, Random, 95% CI)	0.05 [0.02, 0.11]
2.1 Vaginal misoprostol	4	411	Risk Ratio (M-H, Random, 95% CI)	0.16 [0.07, 0.35]
2.2 Oral misoprostol	7	1884	Risk Ratio (M-H, Random, 95% CI)	0.04 [0.02, 0.07]
2.3 Vaginal + oral misoprostol	1	80	Risk Ratio (M-H, Random, 95% CI)	0.04 [0.01, 0.18]
2.4 Rectal misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2.5 Sublingual misoprostol	1	695	Risk Ratio (M-H, Random, 95% CI)	0.02 [0.01, 0.04]
3 Death or serious complication	5	1248	Risk Ratio (M-H, Random, 95% CI)	1.0 [0.04, 22.64]
3.1 Vaginal misoprostol	2	132	Risk Ratio (M-H, Random, 95% CI)	1.0 [0.04, 22.64]
3.2 Oral misoprostol	2	421	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
3.3 Vaginal + oral misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
3.4 Rectal misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
3.5 Sublingual misoprostol	1	695	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
4 Unplanned surgical intervention	11	2690	Risk Ratio (M-H, Random, 95% CI)	5.03 [2.71, 9.35]
4.1 Vaginal misoprostol	4	411	Risk Ratio (M-H, Random, 95% CI)	4.29 [1.24, 14.87]
4.2 Oral misoprostol	6	1584	Risk Ratio (M-H, Random, 95% CI)	5.25 [2.07, 13.32]
4.3 Vaginal + oral misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
4.4 Rectal misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
4.5 Sublingual misoprostol	1	695	Risk Ratio (M-H, Random, 95% CI)	5.98 [0.72, 49.43]
5 Blood transfusion	4		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
5.1 Vaginal misoprostol	3	241	Risk Ratio (M-H, Random, 95% CI)	1.73 [0.19, 16.08]
5.2 Oral misoprostol	1	189	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5.3 Vaginal + oral misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5.4 Rectal misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5.5 Sublingual misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6 Blood loss	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
6.1 Vaginal misoprostol	1	96	Mean Difference (IV, Random, 95% CI)	0.03 [-0.02, 0.08]
6.2 Oral misoprostol	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6.3 Vaginal + oral misoprostol	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6.4 Rectal misoprostol	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6.5 Sublingual misoprostol	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
7 Anaemia	2	731	Risk Ratio (M-H, Random, 95% CI)	0.83 [0.17, 4.12]
7.1 Vaginal misoprostol	1	36	Risk Ratio (M-H, Random, 95% CI)	1.71 [0.24, 12.24]
7.2 Oral misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.3 Vaginal + oral misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.4 Rectal misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.5 Sublingual misoprostol	1	695	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.03, 3.18]
8 Days of bleeding	3	211	Mean Difference (IV, Random, 95% CI)	2.12 [1.18, 3.07]
8.1 Vaginal misoprostol	2	131	Mean Difference (IV, Random, 95% CI)	2.76 [1.55, 3.97]
8.2 Oral misoprostol	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
8.3 Vaginal + oral misoprostol	1	80	Mean Difference (IV, Random, 95% CI)	1.55 [0.58, 2.52]
8.4 Rectal misoprostol	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

8.5 Sublingual misoprostol	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
9 Pain relief	4	525	Risk Ratio (M-H, Random, 95% CI)	1.48 [0.67, 3.25]
9.1 Vaginal misoprostol	3	313	Risk Ratio (M-H, Random, 95% CI)	1.64 [1.05, 2.55]
9.2 Oral misoprostol	1	212	Risk Ratio (M-H, Random, 95% CI)	0.85 [0.77, 0.92]
9.3 Vaginal + oral misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9.4 Rectal misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9.5 Sublingual misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10 Pelvic infection < 14 days	7	907	Risk Ratio (M-H, Random, 95% CI)	0.70 [0.25, 1.99]
10.1 Vaginal misoprostol	4	338	Risk Ratio (M-H, Random, 95% CI)	1.14 [0.29, 4.44]
10.2 Oral misoprostol	2	489	Risk Ratio (M-H, Random, 95% CI)	0.26 [0.03, 2.41]
10.3 Vaginal + oral misoprostol	1	80	Risk Ratio (M-H, Random, 95% CI)	0.5 [0.05, 5.30]
10.4 Rectal misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.5 Sublingual misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11 Cervical damage	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
11.1 Vaginal misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11.2 Oral misoprostol	1	189	Risk Ratio (M-H, Random, 95% CI)	0.07 [0.00, 1.25]
11.3 Vaginal + oral misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11.4 Rectal misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11.5 Sublingual misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12 Digestive disorders	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
12.1 Vaginal misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.2 Oral misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.3 Vaginal + oral misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.4 Rectal misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.5 Sublingual misoprostol	1	516	Risk Ratio (M-H, Random, 95% CI)	3.90 [1.81, 8.42]
13 Women's views/acceptability of method	9	3349	Risk Ratio (M-H, Random, 95% CI)	1.00 [0.99, 1.00]
13.1 Vaginal misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
13.2 Oral misoprostol	7	1875	Risk Ratio (M-H, Random, 95% CI)	1.00 [0.99, 1.00]
13.3 Vaginal + oral misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
13.4 Rectal misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
13.5 Sublingual misoprostol	2	1474	Risk Ratio (M-H, Random, 95% CI)	1.00 [0.98, 1.01]
14 Women's views/satisfaction - continuous data	2		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
14.1 Vaginal misoprostol	2	131	Std. Mean Difference (IV, Random, 95% CI)	1.01 [0.01, 2.00]
14.2 Oral misoprostol	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
14.3 Vaginal + oral misoprostol	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
14.4 Rectal misoprostol	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
14.5 Sublingual misoprostol	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
15 Nausea	11	3015	Risk Ratio (M-H, Random, 95% CI)	2.50 [1.53, 4.09]
15.1 Vaginal misoprostol	3	156	Risk Ratio (M-H, Random, 95% CI)	1.46 [0.61, 3.48]
15.2 Oral misoprostol	6	1700	Risk Ratio (M-H, Random, 95% CI)	2.97 [1.54, 5.74]
15.3 Vaginal + oral misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
15.4 Rectal misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
15.5 Sublingual misoprostol	2	1159	Risk Ratio (M-H, Random, 95% CI)	2.85 [0.70, 11.53]
16 Vomiting	10	2977	Risk Ratio (M-H, Random, 95% CI)	1.97 [1.36, 2.85]

16.1 Vaginal misoprostol	2	131	Risk Ratio (M-H, Random, 95% CI)	1.26 [0.12, 13.73]
16.2 Oral misoprostol	6	1687	Risk Ratio (M-H, Random, 95% CI)	1.84 [1.07, 3.14]
16.3 Vaginal + oral misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
16.4 Rectal misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
16.5 Sublingual misoprostol	2	1159	Risk Ratio (M-H, Random, 95% CI)	2.90 [0.84, 9.96]
17 Diarrhoea	4	757	Risk Ratio (M-H, Random, 95% CI)	4.82 [1.09, 21.32]
17.1 Vaginal misoprostol	2	131	Risk Ratio (M-H, Random, 95% CI)	4.09 [0.51, 32.97]
17.2 Oral misoprostol	2	626	Risk Ratio (M-H, Random, 95% CI)	5.72 [0.69, 47.40]
17.3 Vaginal + oral misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
17.4 Rectal misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
17.5 Sublingual misoprostol	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Comparison 3. Vaginal misoprostol versus expectant care

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Complete miscarriage	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 Gestation < 13 weeks	2	150	Risk Ratio (M-H, Random, 95% CI)	1.23 [0.72, 2.10]
1.2 Geststion 13-23 weeks	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 Gestation not specified	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2 Surgical evacuation	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 Gestation < 13 weeks	2	308	Risk Ratio (M-H, Random, 95% CI)	0.62 [0.17, 2.26]
2.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2.3 Gestation not specified	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
3 Death or serious complication	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 Gestation < 13 weeks	1	126	Risk Ratio (M-H, Fixed, 95% CI)	2.91 [0.12, 70.05]
3.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Unplanned surgical intervention	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
4.1 Gestation < 13 weeks	2	308	Risk Ratio (M-H, Random, 95% CI)	0.62 [0.17, 2.26]
4.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
4.3 Gestation not specified	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5 Blood transfusion	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
5.1 Gestation < 13 weeks	3	332	Risk Ratio (M-H, Fixed, 95% CI)	3.07 [0.13, 74.28]
5.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6 Pain relief	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
6.1 Gestation < 13 weeks	2	308	Risk Ratio (M-H, Random, 95% CI)	1.12 [0.67, 1.88]
6.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6.3 Gestation not specified	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7 Pelvic infection < 14 days	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
7.1 Gestation < 13 weeks	3	333	Risk Ratio (M-H, Fixed, 95% CI)	2.81 [0.77, 10.33]
7.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Comparison 4. Vaginal misoprostol versus surgery

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Complete miscarriage	5		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Gestation < 13 weeks	5	364	Risk Ratio (M-H, Fixed, 95% CI)	0.89 [0.84, 0.95]
1.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Surgical evacuation	4		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 Gestation < 13 weeks	4	411	Risk Ratio (M-H, Random, 95% CI)	0.16 [0.07, 0.35]
2.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2.3 Gestation not specified	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
3 Death or serious complication	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 Gestation < 13 weeks	2	132	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.04, 22.64]
3.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Unplanned surgical intervention	4		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
4.1 Gestation < 13 weeks	4	411	Risk Ratio (M-H, Random, 95% CI)	4.29 [1.24, 14.87]
4.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
4.3 Gestation not specified	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5 Blood transfusion	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
5.1 Gestation < 13 weeks	3	241	Risk Ratio (M-H, Fixed, 95% CI)	1.82 [0.21, 15.70]
5.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6 Anaemia	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
6.1 Gestation < 13 weeks	1	36	Risk Ratio (M-H, Fixed, 95% CI)	1.71 [0.24, 12.24]
6.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Days of bleeding	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
7.1 Gestation < 13 weeks	2	131	Mean Difference (IV, Fixed, 95% CI)	2.76 [1.55, 3.97]
7.2 Gestation 13-23 weeks	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.3 Gestation not specified	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Pain relief	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
8.1 Gestation < 13 weeks	3	313	Risk Ratio (M-H, Fixed, 95% CI)	1.75 [1.21, 2.54]
8.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9 Pelvic infection < 14 days	4		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
9.1 Gestation < 13 weeks	4	338	Risk Ratio (M-H, Fixed, 95% CI)	1.27 [0.37, 4.42]
9.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10 Women's views/satisfaction - continuous data	2		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
10.1 Gestation < 13 weeks	2	131	Std. Mean Difference (IV, Random, 95% CI)	1.01 [0.01, 2.00]
10.2 Gestation 13-23 weeks	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
10.3 Gestation not specified	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
11 Nausea	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
11.1 Gestation < 13 weeks	3	156	Risk Ratio (M-H, Fixed, 95% CI)	1.37 [0.58, 3.22]
11.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12 Vomiting	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
12.1 Gestation < 13 weeks	2	131	Risk Ratio (M-H, Fixed, 95% CI)	1.48 [0.25, 8.93]

12.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13 Diarrhoea	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
13.1 Gestation < 13 weeks	2	131	Risk Ratio (M-H, Fixed, 95% CI)	4.30 [0.52, 35.36]
13.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Comparison 5. Oral misoprostol versus surgery

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Complete miscarriage	7		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 Gestation < 13 weeks	7	1884	Risk Ratio (M-H, Random, 95% CI)	0.98 [0.95, 1.00]
1.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 Gestation not specified	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2 Surgical evacuation	7		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 Gestation < 13 weeks	7	1884	Risk Ratio (M-H, Random, 95% CI)	0.04 [0.02, 0.07]
2.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2.3 Gestation not specified	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
3 Unplanned surgical intervention	6		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 Gestation < 13 weeks	6	1584	Risk Ratio (M-H, Fixed, 95% CI)	6.27 [2.57, 15.31]
3.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Blood transfusion	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 Gestation < 13 weeks	1	189	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Pain relief	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
5.1 Gestation < 13 weeks	1	212	Risk Ratio (M-H, Fixed, 95% CI)	0.85 [0.77, 0.92]
5.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6 Pelvic infection	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
6.1 Gestation < 13 weeks	2	489	Risk Ratio (M-H, Fixed, 95% CI)	0.26 [0.03, 2.41]
6.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Cervical damage	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
7.1 Gestation < 13 weeks	1	189	Risk Ratio (M-H, Fixed, 95% CI)	0.07 [0.00, 1.25]
7.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Women's views/acceptability of method	7		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
8.1 Gestation < 13 weeks	7	1875	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.98, 1.01]
8.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9 Nausea	6		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
9.1 Gestation < 13 weeks	6	1700	Risk Ratio (M-H, Fixed, 95% CI)	3.24 [2.10, 4.98]
9.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10 Vomiting	6		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only

10.1 Gestation < 13 weeks	6	1687	Risk Ratio (M-H, Fixed, 95% CI)	1.99 [1.18, 3.34]
10.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11 Diarrhoea	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
11.1 Gestation < 13 weeks	2	626	Risk Ratio (M-H, Fixed, 95% CI)	5.79 [0.70, 47.64]
11.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Comparison 6. Vaginal + oral misoprostol versus surgery

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Complete miscarriage	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Gestation < 13 weeks	1	80	Risk Ratio (M-H, Fixed, 95% CI)	0.95 [0.87, 1.04]
1.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Surgical evacuation	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 Gestation < 13 weeks	1	80	Risk Ratio (M-H, Fixed, 95% CI)	0.04 [0.01, 0.18]
2.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Days of bleeding	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3.1 Gestation < 13 weeks	1	80	Mean Difference (IV, Fixed, 95% CI)	1.55 [0.58, 2.52]
3.2 Gestation 13-23 weeks	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.3 Gestation not specified	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Pelvic infection	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 Gestation < 13 weeks	1	80	Risk Ratio (M-H, Fixed, 95% CI)	0.5 [0.05, 5.30]
4.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Comparison 7. Sublingual misoprostol versus surgery

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Complete miscarriage	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Gestation < 13 weeks	2	1534	Risk Ratio (M-H, Fixed, 95% CI)	0.96 [0.95, 0.98]
1.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Surgical evacuation	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 Gestation <13 weeks	1	695	Risk Ratio (M-H, Fixed, 95% CI)	0.02 [0.01, 0.04]
2.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Unplanned surgical intervention	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 Gestation < 13 weeks	1	695	Risk Ratio (M-H, Fixed, 95% CI)	5.98 [0.72, 49.43]
3.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

4 Anaemia	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 Gestation < 13 weeks	1	695	Risk Ratio (M-H, Fixed, 95% CI)	0.33 [0.03, 3.18]
4.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Digestive disorders	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
5.1 Gestation < 13 weeks	1	516	Risk Ratio (M-H, Fixed, 95% CI)	3.90 [1.81, 8.42]
5.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6 Women's views/acceptability of method	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
6.1 Gestation < 13 weeks	2	1474	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.98, 1.01]
6.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Nausea	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
7.1 Gestation < 13 weeks	2	1159	Risk Ratio (M-H, Fixed, 95% CI)	1.86 [1.48, 2.32]
7.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Vomiting	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
8.1 Gestation < 13 weeks	2	1159	Risk Ratio (M-H, Fixed, 95% CI)	2.42 [1.43, 4.10]
8.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Comparison 8. Vaginal misoprostol versus oral misoprostol

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Complete miscarriage	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Gestation < 13 weeks	1	198	Risk Ratio (M-H, Fixed, 95% CI)	0.94 [0.76, 1.16]
1.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Surgical evacuation	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 Gestation < 13 weeks	1	198	Risk Ratio (M-H, Fixed, 95% CI)	1.11 [0.77, 1.60]
2.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Unplanned surgical intervention	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 Gestation < 13 weeks	1	186	Risk Ratio (M-H, Fixed, 95% CI)	0.36 [0.01, 8.80]
3.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Pain relief	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 Gestation < 13 weeks	1	186	Risk Ratio (M-H, Fixed, 95% CI)	1.43 [0.93, 2.17]
4.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Nausea	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
5.1 Gestation < 13 weeks	1	198	Risk Ratio (M-H, Fixed, 95% CI)	0.63 [0.26, 1.54]
5.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6 Vomiting	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
6.1 Gestation < 13 weeks	1	198	Risk Ratio (M-H, Fixed, 95% CI)	0.36 [0.07, 1.75]
6.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

6.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Diarrhoea	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
7.1 Gestation < 13 weeks	1	198	Risk Ratio (M-H, Fixed, 95% CI)	0.21 [0.12, 0.36]
7.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Comparison 9. Oral misoprostol: 600 ug versus 1200 ug

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Complete miscarriage	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Gestation < 13 weeks	2	464	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.93, 1.07]
1.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Surgical evacuation	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 Gestation < 13 weeks	1	295	Risk Ratio (M-H, Fixed, 95% CI)	0.76 [0.29, 1.99]
2.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Death or serious complication	1	295	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.1 Gestation < 13 weeks	1	295	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Unplanned surgical intervention	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 Gestation < 13 weeks	1	295	Risk Ratio (M-H, Fixed, 95% CI)	0.76 [0.29, 1.99]
4.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Women's views/acceptability of method	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
5.1 Gestation < 13 weeks	2	460	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.96, 1.09]
5.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6 Nausea	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
6.1 Gestation < 13 weeks	2	463	Risk Ratio (M-H, Random, 95% CI)	1.19 [0.57, 2.46]
6.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6.3 Gestation not specified	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7 Vomiting	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
7.1 Gestation < 13 weeks	2	463	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.60, 1.72]
7.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Diarrhoea	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
8.1 Gestation < 13 weeks	1	294	Risk Ratio (M-H, Fixed, 95% CI)	0.73 [0.55, 0.97]
8.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Comparison 10. Oral mifepristone + vaginal misoprostol versus surgery

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Complete miscarriage	1	19	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.77, 1.31]
1.1 Gestation < 13 weeks	1	16	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.78, 1.27]
1.2 Gestation 13-23 weeks	1	3	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.39, 2.58]
1.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Pelvic infection < 14 days	1	19	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.1 Gestation < 13 weeks	1	16	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.2 Gestation 13-23 weeks	1	3	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Comparison 11. Vaginal prostaglandin E1 (gemeprost) versus surgery

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Unplanned surgical intervention	1	34	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.1 Gestation < 13 weeks	1	34	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Comparison 12. Sublingual misoprostol versus oral misoprostol

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Complete miscarriage	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Gestation < 13 weeks	2	358	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.94, 1.05]
1.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Surgical evacuation	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 Gestation < 13 weeks	1	294	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.39, 2.63]
2.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Death or serious complication	2	358	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.1 Gestation < 13 weeks	2	358	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Nausea	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 Gestation < 13 weeks	2	358	Risk Ratio (M-H, Fixed, 95% CI)	0.78 [0.49, 1.23]
4.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Vomiting	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only

5.1 Gestation < 13 weeks	2	358	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.14, 7.10]
5.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6 Diarrhoea	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
6.1 Gestation < 13 weeks	2	358	Risk Ratio (M-H, Fixed, 95% CI)	1.58 [0.66, 3.76]
6.2 Gestation 13-23 weeks	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.3 Gestation not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Women's views/acceptability of method	2	358	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.95, 1.03]

WHAT'S NEW

Last assessed as up-to-date: 13 May 2016.

Date	Event	Description
13 May 2016	New search has been performed	Search updated and 21 new reports were identified. Of the 21 new reports, four additional trials have been included in the review update
13 May 2016	New citation required but conclusions have not changed	The inclusion of the four new studies has not changed the overall conclusions of the review

HISTORY

Protocol first published: Issue 3, 2008

Review first published: Issue 1, 2010

Date	Event	Description
7 January 2013	New citation required but conclusions have not changed	The inclusion of five new studies has not changed the overall conclusions of the review
30 November 2012	New search has been performed	Search updated. Thie review has been updated. Five new trials have been included (Dabash 2010, Diop 2009, Montesinos 2011, Paritakul 2010, Taylor 2011), and 21 new trials have been excluded. This updated review is now comprised of 20 included studies (involving 4208 women), 135 excluded studies, one ongoing study (Yu 2000a) and one other study that is awaiting classification (ISRCTN65305620). The methods text has been updated and we have added a 'Summary of findings' table

(*Continued*)

23 July 2012	Amended	Search updated. Thirty reports added to Studies awaiting classification

CONTRIBUTIONS OF AUTHORS

JP Neilson, J Vazquez, and M Hickey prepared the first draft of the Background section of the original publication. L Dou did the data extraction. L Dou checked the data and all authors checked the text and contributed to the discussions and conclusions. For the update, trials were assessed for inclusion and data were extracted independently by C Kim and S Barnard. All review authors reviewed the final text.

DECLARATIONS OF INTEREST

Caron Kim: This author reports no conflicts of interest.

Sharmani Barnard: This author reports no conflicts of interest.

James P Neilson: This author reports no conflicts of interest.

Martha Hickey: This author reports no conflicts of interest.

Juan C Vazquez: This author reports no conflicts of interest.

Lixia Dou: This author reports no conflicts of interest.

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Internal sources

- The University of Liverpool, UK.

External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We have modified the wording in the Methods sections for Assessment of heterogeneity, Assessment of reporting biases, and Data synthesis to update them with the new methods being used by Cochrane Pregnancy and Childbirth, developed in conjunction with Cochrane Pregnancy and Childbirth's statisticians, Simon Gates and Richard Riley. We have used these new methods in the review.

We have added GRADE methods for assessing the quality of the evidence for this update (2016) and the secondary outcomes death and serious morbidity have been removed as both of these appear in the composite primary outcome "Death or serious complications".

INDEX TERMS

Medical Subject Headings (MeSH)

*Watchful Waiting; Abortifacient Agents, Nonsteroidal [*administration & dosage; adverse effects]; Abortion, Incomplete [*therapy]; Administration, Intravaginal; Administration, Oral; Diarrhea [chemically induced]; Extraction, Obstetrical [*methods]; Gestational Age; Misoprostol [*administration & dosage; adverse effects]; Nausea [chemically induced]; Pregnancy Trimester, First; Randomized Controlled Trials as Topic; Vomiting [chemically induced]

MeSH check words

Female; Humans; Pregnancy